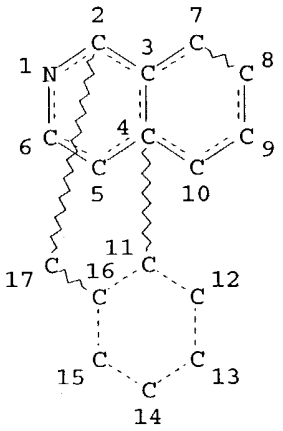
10/049,472
STIC Search
Notes
12/3/04

=> d que l29
L1 STR



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DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
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NUMBER OF NODES IS 17

STEREO ATTRIBUTES: NONE
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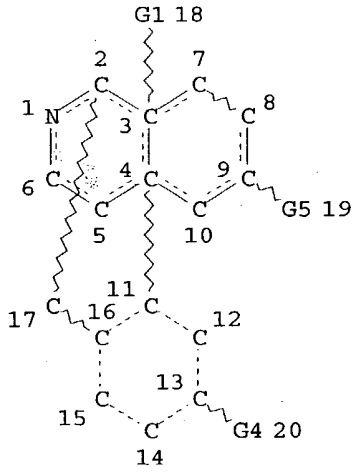

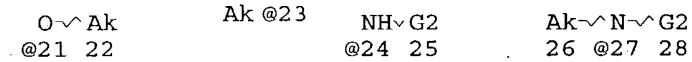

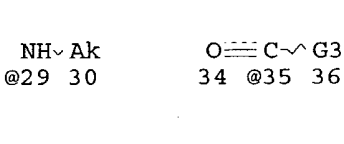

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VAR G2=23/35
VAR G3=H/PH/23
VAR G4=H/OH/31/21
VAR G5=37/38/39
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CONNECT IS E1 RC AT 22
CONNECT IS E1 RC AT 23
CONNECT IS E1 RC AT 26
CONNECT IS E1 RC AT 30
CONNECT IS E1 RC AT 33
CONNECT IS E2 RC AT 37
CONNECT IS M2 RC AT 38
CONNECT IS E2 RC AT 39
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
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STEREO ATTRIBUTES: NONE
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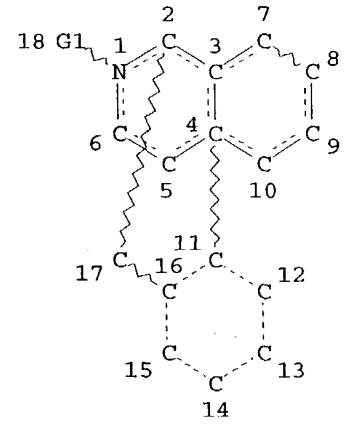
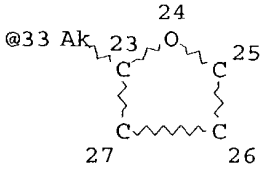
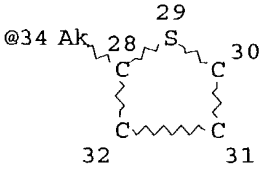
L5 STR



Ak @19 Cb @20

Ak Cb
@21 22





VAR G1=19/20/21/33/34
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CONNECT IS E2 RC AT 21
CONNECT IS E1 RC AT 22
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- IS E2 RC AT 26
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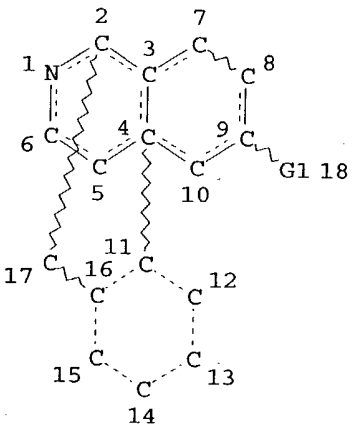
CONNECT IS E2 RC AT 34
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 34

STEREO ATTRIBUTES: NONE
L6 2736 SEA FILE=REGISTRY SUB=L4 SSS FUL L5
L7 STR



G2-N-G4
42 @43 44

O-G4
@45 46

S-G4
@47 48

Ak @65

G2-N-SO2-G4
49 @50 51 52

O-SO2-G4
@53 54 55

S-SO2-G4
@56 57 58

59
G3
G2-N-C-G4
19 @20 21 22

Cb @66
60
G3

N-G2
@67 68

61
G3

62
G3

63
G3

Page 1-A

O-C-G4
@23 24 25

S-C-G4
@26 27 28

G2-N-C-G3-G4
29 @30 31 32 33

O-C-G3-G4
@34 35 36 37

64
G3
S-C-G3-G4
@38 39 40 41

Page 2-A
VAR G1=20/23/26/30/34/38/43/45/47/50/53/56
VAR G2=H/65/66
VAR G3=67/O/S
VAR G4=AK/CB
NODE ATTRIBUTES:
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DEFAULT MLEVEL IS ATOM
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DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 68

STEREO ATTRIBUTES: NONE
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L21 664 SEA FILE=HCAPLUS ABB=ON PLU=ON L8(L)(BAC OR DMA OR PAC OR PKT OR THU)/RL
L27 4434 SEA FILE=HCAPLUS ABB=ON PLU=ON ANALGESICS+OLD,NT/CT(L)NEUR?
L28 3708 SEA FILE=HCAPLUS ABB=ON PLU=ON PAIN+NT/CT(L)NEUR?
L29 26 SEA FILE=HCAPLUS ABB=ON PLU=ON L21 AND (L27 OR L28)

=> d l29 ibib abs hitind hitstr 1-26

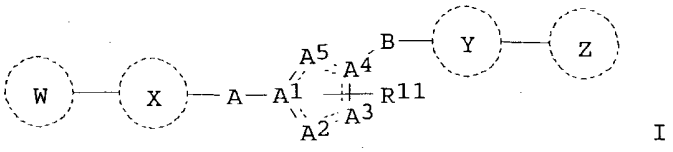
L29 ANSWER 1 OF 26 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:878275 HCAPLUS
DOCUMENT NUMBER: 141:366235
TITLE: Preparation of diaryl substituted triazole modulators of metabotropic glutamate receptor-5
INVENTOR(S): Cosford, Nicholas D. P.; Roppe, Jeffrey R.; Tehrani, Lida R.; Wang, Bowei
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 42 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004089306	A2	20041021	WO 2004-US9750	20040331

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2003-462796P P 20030404

GI



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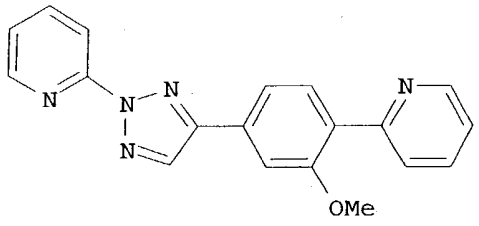


II

AB Title compds. represented by the formula I [wherein X, Y = independently (hetero)aryl, and at least one of X and Y is a heteroaryl with N adjacent to the position of attachment to A or B; A1-A5 = independently N or C, three of them are N, and one of A1 and A4 must be N, but not both A1 and A4 are N; A, B = independently (hetero)alkyl, alkylsulfonylalkyl, alkylcarbonylalkyl, etc.; W, Z = independently (un)substituted (hetero)cycloalkyl, alkyl(hetero)aryl; R11 = halo, alkyl, alkoxyl, etc.; and pharmaceutically acceptable salts thereof] were prepared as modulators of metabotropic glutamate receptor-5 (mGluR5). For example, reaction of 2-[2-methoxy-4-(1H-1,2,3-triazol-4-yl)phenyl]pyridine with 1-fluoropyridinium triflate gave II. The prepared I were tested for mGluR5 inhibitory activity with IC50 value of less than 10 μM in the calcium flux assay or inhibition of >50 % at a concentration of 100 μM in the PI assay. Thus, I and their pharmaceutical compns. are useful as modulators of mGluR5 for the treatment of panic, and bipolar disorder, as well as in the treatment of psychiatric and mood disorders such as, for example, schizophrenia, anxiety, depression, panic, and bipolar disorder, as well as in the treatment of pain, Parkinson's disease, cognitive dysfunction, epilepsy, circadian rhythm disorders, obesity, drug addiction, drug abuse, drug withdrawal and other diseases (no data).

IC ICM A61K

CC 28-10 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1, 63

IT **Nerve, disease**
Pain
(**neuralgia**; preparation of diaryl substituted triazole modulators of metabotropic glutamate receptor-5)

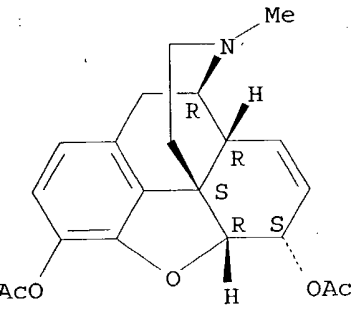
IT **561-27-3**, Heroin
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(substituting drug, combination therapy agent; preparation of diaryl substituted triazole modulators of metabotropic glutamate receptor-5)

IT **561-27-3**, Heroin
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(substituting drug, combination therapy agent; preparation of diaryl substituted triazole modulators of metabotropic glutamate receptor-5)

RN 561-27-3 HCAPLUS

CN Morphinan-3,6-diol, 7,8-didehydro-4,5-epoxy-17-methyl-, (5α,6α)-, diacetate (ester) (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L29 ANSWER 2 OF 26 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:878273 HCAPLUS
DOCUMENT NUMBER: 141:366220
TITLE: Preparation of diaryl substituted pyrazole modulators of metabotropic glutamate receptor-5
INVENTOR(S): Cosford, Nicholas D. P.; Eastman, Brian W.; Huang, Dehua; Smith, Nicholas D.; Tehrani, Lida R.
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 72 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004089303	A2	20041021	WO 2004-US11651	20040330

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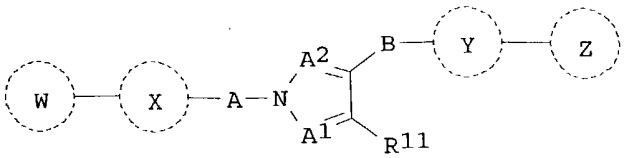
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2003-460094P P 20030403
GI



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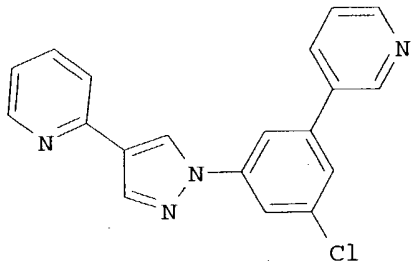


II

AB Title compds. represented by the formula I [wherein X, Y = independently (hetero)aryl, and at least one of X and Y is a heteroaryl with N adjacent to the position of attachment to A or B; A, B = independently (hetero)alkyl, alkylsulfonylalkyl, alkylcarbonylalkyl, etc.; W, Z = independently (un)substituted (hetero)cycloalkyl, alkyl(hetero)aryl; one of A1 and A2 is N, the other in (un)substituted C; R11 = halo, alkyl, alkoxyl, amino(di)(alkyl); and pharmaceutically acceptable salts thereof] were prepared as modulators of metabotropic glutamate receptor-5 (mGluR5). For example, reaction of 2-(2-pyridyl)malondialdehyde with hydrazine hydrate (60%), followed by substitution with 1-bromo-3-chloro-5-fluorobenzene (45%) and coupling reaction with pyridin-3-ylboronic acid (80%), gave II. The prepared I were tested for mGluR5 inhibitory activity with IC50 value of about 2 μM in the calcium flux assay. Thus, I and their pharmaceutical compns. are useful as modulators of mGluR5 for the treatment of panic, and bipolar disorder, as well as in the treatment of psychiatric and mood disorders such as, for example, schizophrenia, anxiety, depression, panic, and bipolar disorder, as well as in the treatment of pain, Parkinson's disease, cognitive dysfunction, epilepsy, circadian rhythm disorders, obesity, drug addiction, drug abuse, drug withdrawal and other diseases (no data).

IC ICM A61K

CC 28-8 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1, 63

IT **Nerve, disease**
Pain
(**neuralgia**; preparation of diaryl pyrazole modulators of metabotropic glutamate receptor-5)

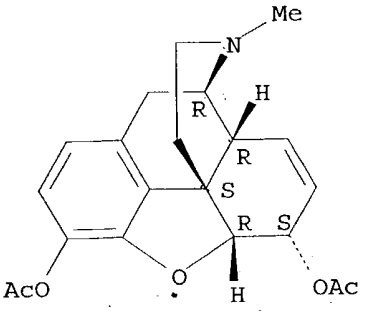
IT **561-27-3**, Heroin
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(substituting drug, combination therapy agent; preparation of diaryl pyrazole modulators of metabotropic glutamate receptor-5)

IT **561-27-3**, Heroin
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(substituting drug, combination therapy agent; preparation of diaryl pyrazole modulators of metabotropic glutamate receptor-5)

RN 561-27-3 HCAPLUS

CN Morphinan-3,6-diol, 7,8-didehydro-4,5-epoxy-17-methyl-, (5α,6α)-, diacetate (ester) (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L29 ANSWER 3 OF 26 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:872663 HCAPLUS
DOCUMENT NUMBER: 141:366129
TITLE: Preparation of diaryl substituted pyrrole modulators of metabotropic glutamate receptor-5
INVENTOR(S): Cosford, Nicholas D. P.; Huang, Dehua; Roppe, Jeffrey R.; Smith, Nicholas D.; Tehrani, Lida R.
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 57 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004089308	A2	20041021	WO 2004-US9845	20040331

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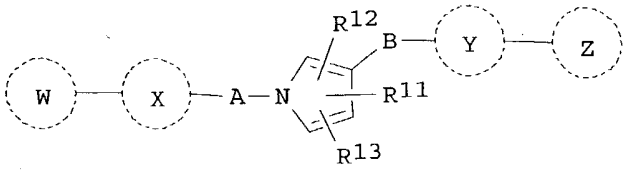
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2003-460085P P 20030404
GI



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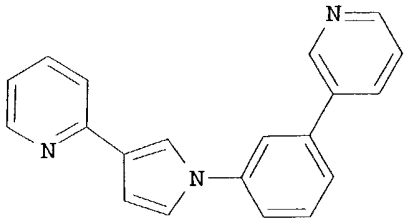


II

AB Title compds. represented by the formula I [wherein X, Y = independently (hetero)aryl, and at least one of X and Y is a heteroaryl with N adjacent to the position of attachment to A or B; A, B = independently (hetero)alkyl, alkylsulfonylalkyl, alkylcarbonylalkyl, etc.; W, Z = independently (un)substituted (hetero)cycloalkyl, alkyl(hetero)aryl; R11, R12, R13 = independently halo, alkyl, alkoxy, etc.; and pharmaceutically acceptable salts thereof] were prepared as modulators of metabotropic glutamate receptor-5 (mGluR5). For example, reaction of 2-(1H-pyrrol-3-yl)pyridine with 3-(3-iodophenyl)pyridine gave II. The prepared I were tested for mGluR5 inhibitory activity with IC50 value of less than 10 μM in the calcium flux assay or inhibition at a concentration of 100μM in the PI assay. Thus, I and their pharmaceutical compns. are useful as modulators of mGluR5 for the treatment of panic, and bipolar disorder, as well as in the treatment of psychiatric and mood disorders such as, for example, schizophrenia, anxiety, depression, panic, and bipolar disorder, as well as in the treatment of pain, Parkinson's disease, cognitive dysfunction, epilepsy, circadian rhythm disorders, obesity, drug addiction, drug abuse, drug withdrawal and other diseases (no data).

IC ICM A61K

CC 27-16 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1, 63

IT **Nerve, disease**
Pain
(**neuralgia**; preparation of diaryl substituted pyrrole modulators of metabotropic glutamate receptor-5)

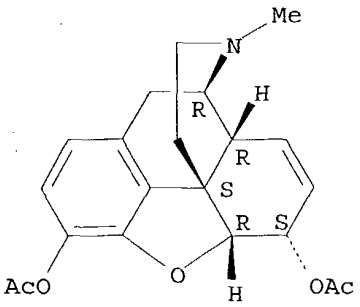
IT **561-27-3**, Heroin
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(substituting drug, combination therapy agent; preparation of diaryl substituted pyrrole modulators of metabotropic glutamate receptor-5)

IT **561-27-3**, Heroin
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(substituting drug, combination therapy agent; preparation of diaryl substituted pyrrole modulators of metabotropic glutamate receptor-5)

RN 561-27-3 HCAPLUS

CN Morphinan-3,6-diol, 7,8-didehydro-4,5-epoxy-17-methyl-(5α,6α)-, diacetate (ester) (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L29 ANSWER 4 OF 26 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:825130 HCAPLUS
DOCUMENT NUMBER: 141:307586
TITLE: Method for the treatment of pain with opioid analgesics minimizing their side effects by administration of devazepide
INVENTOR(S): Gibson, Karen
PATENT ASSIGNEE(S): UK
SOURCE: U.S. Pat. Appl. Publ., 6 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004198723	A1	20041007	US 2002-53962	20020122
US 2003139396	A1	20030724	US 2002-108659	20020327
US 2003153592	A1	20030814	US 2003-349431	20030122
US 6713470	B2	20040330		
US 2004167146	A1	20040826	US 2003-622492	20030721
US 2004142959	A1	20040722	US 2004-752411	20040107
PRIORITY APPLN. INFO.:			GB 2002-1367	A 20020122
			US 2002-53962	A2 20020122
			US 2002-108659	A2 20020327
			GB 2002-8129	A 20020409
			US 2003-349431	A2 20030122

AB Method is disclosed for the treatment of a patient undergoing opioid analgesic therapy which comprises minimizing the side effects of the opioid by the administration of a therapeutically effective amount of devazepide.

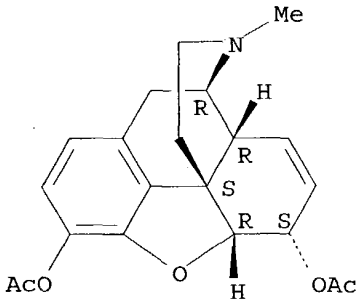
IC ICM A61K031-5513
ICS A61K031-485
NCL 514221000; 514282000
CC 1-11 (Pharmacology)
Section cross-reference(s): 63
IT **Pain**
(**neuropathic**; method for treatment of pain with opioid analgesics minimizing their side effects by administration of devazepide)
IT 52-26-6, Morphine hydrochloride 57-27-2, Morphine, biological studies 57-42-1, Pethidine 64-31-3, Morphine sulphate 76-41-5, Oxymorphone 76-42-6, Oxycodone 76-57-3, Codeine 76-99-3, Methadone 77-07-6, Levorphanol 77-20-3, Alphaprodine 125-28-0, Dihydrocodeine 125-29-1,

Hydrocodone 127-35-5, Phenazocine 143-52-2, Metopon 357-56-2, Dextromoramide 359-83-1, Pentazocine 437-38-7, Fentanyl 465-65-6, Naloxone 466-99-9, Hydromorphone 467-83-4, Dipipanone 467-84-5, Phenadoxone 468-10-0D, Morphinan, derivs. 469-62-5, Dextropropoxyphene **561-27-3**, Heroin 915-30-0, Diphenoxylate 20290-10-2, Morphine-6-glucuronide 20594-83-6, Nalbuphine 27203-92-5, Tramadol 42408-82-2, Butorphanol 52485-79-7, Buprenorphine 54340-58-8, Meptazinol 71195-58-9, Alfentanil 132875-61-7, Remifentanil
RL: ADV (Adverse effect, including toxicity); **PAC (Pharmacological activity)**; **THU (Therapeutic use)**; BIOL (Biological study);
USES (Uses)
(method for treatment of pain with opioid analgesics minimizing their side effects by administration of devazepide)

IT **561-27-3**, Heroin
RL: ADV (Adverse effect, including toxicity); **PAC (Pharmacological activity)**; **THU (Therapeutic use)**; BIOL (Biological study);
USES (Uses)
(method for treatment of pain with opioid analgesics minimizing their side effects by administration of devazepide)

RN 561-27-3 HCAPLUS
CN Morphinan-3,6-diol, 7,8-didehydro-4,5-epoxy-17-methyl-(5α,6α)-, diacetate (ester) (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L29 ANSWER 5 OF 26 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:392451 HCAPLUS
DOCUMENT NUMBER: 140:395537
TITLE: New formulations of injectable particles for intra-articular injection containing therapeutic compositions
INVENTOR(S): Giroux, Karen; Butz, Robert F.
PATENT ASSIGNEE(S): Polymerix Corporation, USA
SOURCE: PCT Int. Appl., 40 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004039355	A1	20040513	WO 2003-US34183	20031028

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE,

GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK,
LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ,
OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM,
TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ,
BY, KG, KZ, MD
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG,
CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC,
NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ,
GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2002-421888P P 20021028

AB The present invention provides new formulations of injectable particles (e.g. microspheres) useful for intra-articular (i.a.) injection. The formulations are made of biocompatible polymers that biodegrade to generate NSAIDs, ad are useful for treating inflamed joints, thus providing safe, long-lasting relief of joint pain and swelling. In one embodiment, the present invention provides an injectable particle, comprising a biodegradable polymer comprising an agent selected from the group consisting of an NSAID, a COX-2 inhibitor, an anesthetic and a narcotic analgesic. Injectable mcirosppheres containing salicylic acid were prepared and their efficacy in reducing joint swelling and serum ovalbumin antibody was shown in rabbits.

IC ICM A61K009-14

CC 63-6 (Pharmaceuticals)

IT **Nerve, disease**
Pain
(**neuralgia**; new formulations of injectable particles for intra-articular injection containing therapeutic compns.)

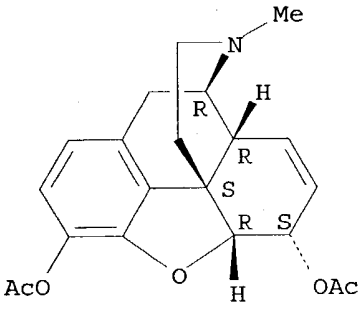
IT 50-36-2, Cocaine 57-27-2, Morphine, biological studies 57-42-1, Meperidine 59-46-1, Procaine 61-68-7, Mefenamic acid 69-72-7, Salicylic acid, biological studies 76-41-5, Oxymorphone 76-42-6, Oxycodone 76-57-3, Codeine 76-99-3, Methadone 77-07-6, Levorphanol 85-79-0, Dibucaine 86-43-1, Propoxycaine 87-28-5, Glycol salicylate 89-57-6, Mesalamine 92-23-9, Leucinocaine 94-09-7, Benzocaine 94-23-5, Parethoxycaine 96-88-8, Mepivacaine 99-43-4, Oxybuprocaine 101-93-9, Phenacaine 125-28-0, Dihydrocodeine 125-29-1, Dihydrocodeinone 133-16-4, Chloroprocaine 136-47-0 136-82-3, Piperocaine 137-58-6, Lidocaine 139-62-8, Cyclomethycaine 140-65-8, Pramoxine 149-16-6, Butacaine 152-02-3, Levallorphan 359-83-1, Pentazocine 437-38-7, Fentanyl 466-99-9, Hydromorphone 469-62-5, Propoxyphene 490-79-9, Gentisic acid 493-76-5, Propanocaine 495-70-5, Meprylcaine 499-67-2, Proxymetacaine 530-78-9, Flufenamic acid 552-94-3, Salsalate **561-27-3**, Heroin 589-44-6, 3-Amino-4-hydroxybutyric acid 599-79-1, Sulfasalazine 644-62-2, Meclofenamic acid 721-50-6, Prilocaine 915-30-0, Diphenoxylate 2210-77-7, Pyrrocaine 2316-64-5, Bromosaligenin 3583-64-0, Bumadizon 3686-58-6, Tolycaine 3785-21-5, Butanilicaine 4394-00-7, Niflumic acid 6740-88-1, Ketamine 7712-50-7, Myrtecaine 13710-19-5, Tolfenamic acid 13912-77-1, Octacaine 14055-89-1, Isobucaine 14521-96-1, Etorphine 15307-86-5, Diclofenac 15722-48-2, Olsalazine 17692-39-6, Fomocaine 18471-20-0, Ditazol 20290-10-2, Morphine-6-glucuronide 20594-83-6, Nalbuphine 22494-42-4, Diflunisal 23049-93-6, Enfenamic acid 23964-58-1, Carticaine 27203-92-5, Tramadol 29908-03-0 30544-47-9, Etofenamate 33996-33-7, Oxaceprol 36292-66-7, Ethylketocyclazocine 36637-18-0, Etidocaine 36981-91-6, Fepradinol 38396-39-3, Bupivacaine 39718-89-3, Alminoprofen 41340-25-4, Etodolac 42408-82-2, Butorphanol 51579-82-9, Amfenac 52443-21-7, Glucamethacin 52485-79-7, Buprenorphine 53597-27-6, Fendosal 53716-49-7, Carprofen 56030-54-7, Sufentanil 58569-55-4, [Met5 enkephalin 58822-25-6, 1-5-β-Neoendorphin (human) 60617-12-1, β-Endorphin

63631-40-3, DADL 64854-64-4, FK 33824 67198-13-4 69671-17-6, α-Neoendorphin 71195-58-9, Alfentanil 74135-04-9, Morphiceptin 75644-90-5 75684-07-0, Bremazocine 77752-00-2, β-Neoendorphin 78123-71-4, DAMGO 83397-56-2, PL 017 84057-95-4, Ropivacaine 85006-82-2, Dynorphin B 87151-85-7, Spiradoline 88161-22-2, Dynorphin A 88373-73-3 89796-99-6, Aceclofenac 91714-94-2, Bromfenac 96744-75-1 103429-31-8, CTOP 110881-59-9 122752-15-2, Deltorphin C 122752-16-3, (Deltorphin II) 132875-61-7, Remifentanil 141801-26-5, Endomorphin-2 170713-75-4, Orphanin FQ 189388-22-5, Endomorphin-1
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(new formulations of injectable particles for intra-articular injection containing therapeutic compns.)

IT **561-27-3**, Heroin
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(new formulations of injectable particles for intra-articular injection containing therapeutic compns.)

RN 561-27-3 HCAPLUS
CN Morphinan-3,6-diol, 7,8-didehydro-4,5-epoxy-17-methyl-, (5α,6α)-, diacetate (ester) (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L29 ANSWER 6 OF 26 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:182525 HCAPLUS
DOCUMENT NUMBER: 140:210804
TITLE: Method of analgesic treatment with devazepide
INVENTOR(S): Jackson, Karen
PATENT ASSIGNEE(S): UK
SOURCE: U.S. Pat. Appl. Publ., 6 pp., Cont.-in-part of U.S. Ser. No. 349,431.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004043990	A1	20040304	US 2003-410311	20030409
US 2003153592	A1	20030814	US 2003-349431	20030122
US 6713470	B2	20040330		
PRIORITY APPLN. INFO.:			GB 2002-8129	A 20020409
			US 2003-349431	A2 20030122
			US 2002-53962	B2 20020122
			US 2002-108659	A2 20020327

AB There is described a method of treatment of a patient requiring analgesic therapy which comprises the administration of an analgesically effective amount of devazepide. There is also described the use of devazepide in the manufacture of an analgesically effective medicament. Ten of seventeen patients had long-term pain relief (5-26 wk) with devazepide. The patients had pain with a neuropathic element and were taking regular, stable doses of strong opioids.

IC ICM A61K031-7052
ICS A61K031-5513; A61K031-485

NCL 514221000; 514023000; 514282000

CC 1-11 (Pharmacology)

IT **Pain**
(**neuropathic**; analgesic treatment with devazepide)

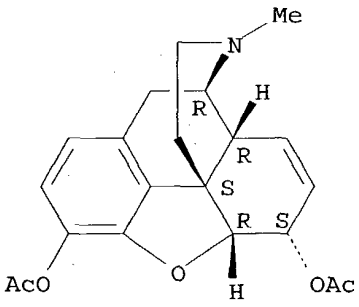
IT 52-26-6 57-27-2, Morphine, biological studies 57-27-2D, Morphine, salts 57-42-1, Meperidine 64-31-3, Morphine sulfate 76-41-5, Oxymorphone 76-42-6, Oxycodone 76-57-3, Codeine 76-99-3, Methadone 77-07-6, Levorphanol 77-20-3, Alphaprodine 125-28-0, Dihydrocodeine 125-29-1, Hydrocodone 127-35-5, Phenazocine 143-52-2, Metopon 357-56-2, Dextromoramide 359-83-1, Pentazocine 437-38-7, Fentanyl 465-65-6, Naloxone 466-99-9, Hydromorphone 467-83-4, Dipipanone 467-84-5, Phenadoxone 469-62-5, Dextropropoxyphene **561-27-3**, Diamorphine 915-30-0, Diphenoxylate 20290-10-2, Morphine-6-glucuronide 20594-83-6, Nalbuphine 27203-92-5, Tramadol 42408-82-2, Butorphanol 52485-79-7, Buprenorphine 54340-58-8, Meptazinol 71195-58-9, Alfentanil 132875-61-7, Remifentanil
RL: BSU (Biological study, unclassified); **PAC (Pharmacological activity)**; **THU (Therapeutic use)**; BIOL (Biological study);
USES (Uses)
(as addnl. analgesic; analgesic treatment with devazepide)

IT **561-27-3**, Diamorphine
RL: BSU (Biological study, unclassified); **PAC (Pharmacological activity)**; **THU (Therapeutic use)**; BIOL (Biological study);
USES (Uses)
(as addnl. analgesic; analgesic treatment with devazepide)

RN 561-27-3 HCAPLUS

CN Morphinan-3,6-diol, 7,8-didehydro-4,5-epoxy-17-methyl-(5α,6α)-, diacetate (ester) (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L29 ANSWER 7 OF 26 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:142816 HCAPLUS
DOCUMENT NUMBER: 140:187398
TITLE: Pharmaceutical formulations containing cannabinoids
INVENTOR(S): Whittle, Brian

PATENT ASSIGNEE(S): UK
SOURCE: U.S. Pat. Appl. Publ., 26 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004034108	A1	20040219	US 2002-218989	20020814
WO 2004016246	A1	20040226	WO 2003-GB3574	20030814

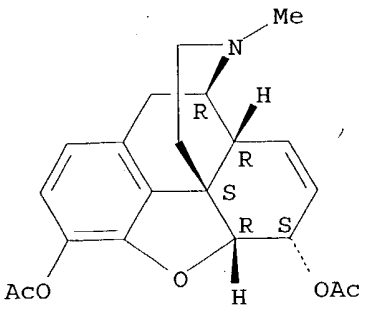
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: GB 2002-18930 A 20020814
US 2002-218989 A 20020814

AB The invention relates to pharmaceutical formulations, and more particularly to formulations containing cannabinoids for administration via a pump action spray. In particular, the invention relates to pharmaceutical formulations, for use in administration of lipophilic drugs via mucosal surfaces, comprising a solvent and a co-solvent, wherein the total amount of solvent and co-solvent present in the formulation is >55% of the formulation and the formulation is free from a self-emulsifying agent and/or a fluorinated propellant. Thus, a composition contained THC 25-50 and CBD 25-50 mg/mL, propylene glycol 0.5, peppermint oil 0.0005 Ethanol (anhydrous) qs to 1 mL.

IC ICM A61F013-00
ICS A61K047-00
NCL 514772000
CC 63-6 (Pharmaceuticals)
IT **Pain**
(**neurogenic**; pharmaceutical formulations containing cannabinoids)
IT 56-81-5, Glycerol, biological studies 57-27-2, Morphine, biological studies 57-42-1, Pethidine 57-55-6, Propylene glycol, biological studies 64-17-5, Ethanol, biological studies 76-57-3, Codeine 76-99-3, Methadone 437-38-7, Fentanyl 521-35-7, Cannabinol **561-27-3**, Diamorphine 846-50-4, Temazepam 1972-08-3, Tetrahydrocannabinol 5957-75-5, Δ8-Tetrahydrocannabinol 13956-29-1, Cannabidiol 20675-51-8, Cannabichromene 24274-48-4, Cannabidivarin 25654-31-3, Cannabigerol 31262-37-0 52485-79-7, Buprenorphine 67035-85-2 71195-58-9, Alfentanil 519002-40-5 658702-43-3
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(pharmaceutical formulations containing cannabinoids)
IT **561-27-3**, Diamorphine
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(pharmaceutical formulations containing cannabinoids)
RN 561-27-3 HCAPLUS
CN Morphinan-3,6-diol, 7,8-didehydro-4,5-epoxy-17-methyl-, (5α,6α)-, diacetate (ester) (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L29 ANSWER 8 OF 26 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:836862 HCAPLUS
DOCUMENT NUMBER: 139:302070
TITLE: The use of devazepide as analgesic agent
INVENTOR(S): Jackson, Karen
PATENT ASSIGNEE(S): Ml Laboratories PLC, UK
SOURCE: PCT Int. Appl., 26 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003086409	A1	20031023	WO 2003-GB1514	20030409

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: GB 2002-8129 A 20020409

AB There is described a method of treatment of a patient requiring analgesic therapy which comprises the administration of an analgesically effective amount of devazepide. There is also described the use of devazepide in the manufacture of an analgesically effective medicament.

IC ICM A61K031-5513
ICS A61P025-04; A61P043-00
CC 1-11 (Pharmacology)
IT **Pain**
Skin, disease
(allodynia; treatment of **neuropathic** pain with devazepide and in combination with opioid analgesics)
IT **Analgesics**
Human
(treatment of **neuropathic** pain with devazepide and in combination with opioid analgesics)
IT **Opioids**

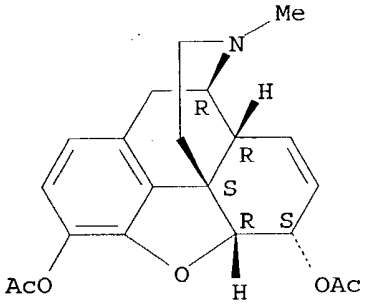
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(treatment of **neuropathic** pain with devazepide and in combination with opioid analgesics)

IT 52-26-6, Morphine hydrochloride 57-27-2, Morphine, biological studies 57-42-1, Meperidine 64-31-3, Morphine sulfate 76-41-5, Oxymorphone 76-42-6, Oxycodone 76-57-3, Codeine 76-99-3, Methadone 77-07-6, Levorphanol 77-20-3, Alphaprodine 125-28-0, Dihydrocodeine 125-29-1, Hydrocodone 127-35-5, Phenazocine 143-52-2, Metopon 357-56-2, Dextromoramide 359-83-1, Pentazocine 437-38-7, Fentanyl 465-65-6, Naloxone 466-99-9, Hydromorphone 467-83-4, Dipipanone 467-84-5, Phenadoxone 469-62-5, Dextropropoxyphene **561-27-3**, Heroin 915-30-0, Diphenoxylate 20290-10-2, Morphine-6-glucuronide **20594-83-6**, Nalbuphine 27203-92-5, Tramadol **42408-82-2**, Butorphanol 52485-79-7, Buprenorphine 54340-58-8, Meptazinol 71195-58-9, Alfentanyl 103420-77-5, Devazepide 124417-48-7D, Hydroxymorphinan, derivs. 132875-61-7, Remifentanyl
RL: **PAC (Pharmacological activity)**; **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(treatment of **neuropathic** pain with devazepide and in combination with opioid analgesics)

IT **561-27-3**, Heroin **20594-83-6**, Nalbuphine **42408-82-2**, Butorphanol
RL: **PAC (Pharmacological activity)**; **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(treatment of **neuropathic** pain with devazepide and in combination with opioid analgesics)

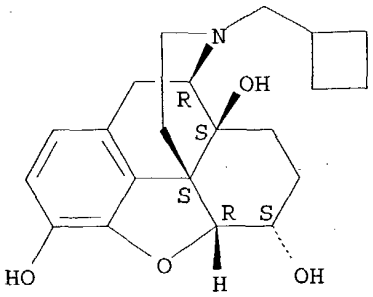
RN 561-27-3 HCAPLUS
CN Morphinan-3,6-diol, 7,8-didehydro-4,5-epoxy-17-methyl-, (5α,6α)-, diacetate (ester) (9CI) (CA INDEX NAME)

Absolute stereochemistry.



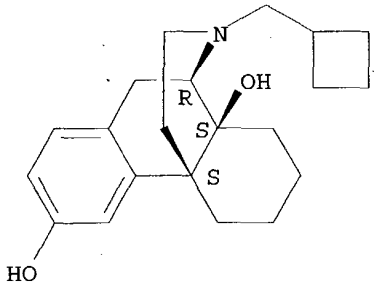
RN 20594-83-6 HCAPLUS
CN Morphinan-3,6,14-triol, 17-(cyclobutylmethyl)-4,5-epoxy-, (5α,6α)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 42408-82-2 HCAPLUS
CN Morphinan-3,14-diol, 17-(cyclobutylmethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L29 ANSWER 9 OF 26 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:678607 HCAPLUS
DOCUMENT NUMBER: 139:173833
TITLE: Use of opioid compound to treat a neurologic or neurogenic disorder
INVENTOR(S): Brooks-Korn, Howard
PATENT ASSIGNEE(S): USA
SOURCE: PCT Int. Appl., 37 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003070175	A2	20030828	WO 2003-US4644	20030214
WO 2003070175	A3	20040408		

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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,

FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2003166670 A1 20030904 US 2003-367386 20030214

PRIORITY APPLN. INFO.: US 2002-357389P P 20020215

AB The invention discloses the use of opioid compds. for treatment of a neurol. or neurogenic disorder. Such neurol. or neurogenic disorders include lingual, pharyngeal, laryngeal, esophageal, urinary bladder sphincter, lumbar-lumbosacral spine, pelvis-pelvic limb paresis or paralysis. The invention provides a unique method of treating the specified disorder by administering a therapeutically effective amount of pharmaceutical formulation comprising an opioid compound

IC ICM A61K

CC 1-11 (Pharmacology)

IT **Opioids**

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(opioid compound for treatment of **neurol**. or **neurogenic** disorder)

IT 57-27-2, Morphine, biological studies 58-74-2, Papaverine 62-67-9, Nalorphine 76-41-5, Oxymorphone 76-42-6, Oxycodone 76-57-3, Codeine 77-15-6, Ethoheptazine 115-37-7, Thebaine 124-90-3, Oxycodone hydrochloride 125-29-1, Hydrocodone 127-35-5, Phenazocine 128-62-1, Noscapine 437-38-7, Fentanyl 465-65-6, Naloxone 466-99-9, Hydromorphone 469-62-5, Propoxyphene **561-27-3**, Heroin 16590-41-3, Naltrexone 27203-92-5, Tramadol 37187-80-7, Metapon

RL: **PAC (Pharmacological activity)**; **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)

(opioid compound for treatment of neurol. or neurogenic disorder)

IT **561-27-3**, Heroin

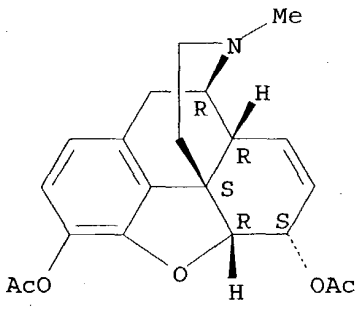
RL: **PAC (Pharmacological activity)**; **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)

(opioid compound for treatment of neurol. or neurogenic disorder)

RN 561-27-3 HCAPLUS

CN Morphinan-3,6-diol, 7,8-didehydro-4,5-epoxy-17-methyl-(5α,6α)-, diacetate (ester) (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L29 ANSWER 10 OF 26 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2002:587081 HCAPLUS

DOCUMENT NUMBER: 138:130994

TITLE: Toxic effects of opioid and stimulant drugs on undifferentiated PC12 cells

AUTHOR(S): Oliveira, M. T.; Rego, A. C.; Morgadinho, M. T.; Macedo, T. R. A.; Oliveira, C. R.

CORPORATE SOURCE: Institute of Biochemistry, Faculty of Medicine and Center for Neuroscience and Cell Biology of Coimbra, University of Coimbra, Coimbra, 3004-504, Port.
SOURCE: Annals of the New York Academy of Sciences (2002), 965(Cellular and Molecular Mechanisms of Drugs of Abuse II), 487-496
CODEN: ANYAA9; ISSN: 0077-8923
PUBLISHER: New York Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Cell death and reactive oxygen species production have been suggested to be involved in neurodegeneration induced by the drugs of abuse. In this study we analyze the toxicity of the following drugs of abuse: heroin, morphine, d-amphetamine, and cocaine in undifferentiated PC12 cells, used as dopaminergic neuronal models. Our data show that opioid drugs (heroin and morphine) are more toxic than stimulant drugs (d-amphetamine and cocaine). Toxic effects induced by heroin are associated with a decrease in intracellular dopamine, an increase in DOPAC levels, and the formation of ROS, whereas toxic effects induced by amphetamine are associated with a decrease in intracellular dopamine and in ATP/ADP levels. In contrast with cocaine, both amphetamine and heroin induced features of apoptosis. The data suggest that the death of cultured PC12 cells induced by the drugs of abuse is correlated with a decrease in intracellular dopamine levels, which can be associated with an increased dopamine turnover and oxidative cell injury.

CC 1-11 (Pharmacology)

IT **Opioids**
RL: ADV (Adverse effect, including toxicity); DMA (Drug mechanism of action); PAC (Pharmacological activity); BIOL (Biological study)
(drugs of abuse toxic effects on dopaminergic **neurons**)

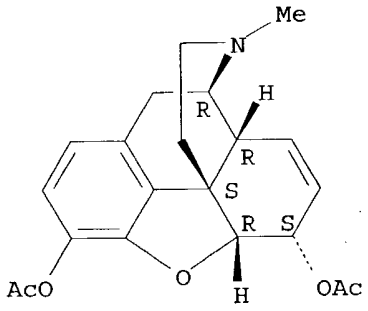
IT 50-36-2, Cocaine 51-64-9 57-27-2, Morphine, biological studies **561-27-3**, Heroin
RL: ADV (Adverse effect, including toxicity); **DMA (Drug mechanism of action)**; **PAC (Pharmacological activity)**; BIOL (Biological study)
(drugs of abuse toxic effects on dopaminergic neurons)

IT **561-27-3**, Heroin
RL: ADV (Adverse effect, including toxicity); **DMA (Drug mechanism of action)**; **PAC (Pharmacological activity)**; BIOL (Biological study)
(drugs of abuse toxic effects on dopaminergic neurons)

RN 561-27-3 HCAPLUS

CN Morphinan-3,6-diol, 7,8-didehydro-4,5-epoxy-17-methyl-, (5α,6α)-, diacetate (ester) (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L29 ANSWER 11 OF 26 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:535645 HCAPLUS
DOCUMENT NUMBER: 138:198093
TITLE: Sulphatoxymelatonin excretion during opiate withdrawal. A preliminary study
AUTHOR(S): Bearn, Jennifer; Gupta, Renu; Stewart, Duncan; English, Judie; Gossop, Michael
CORPORATE SOURCE: National Addiction Centre, South London and Maudsley NHS Trust/Institute of Psychiatry, London, UK
SOURCE: Progress in Neuro-Psychopharmacology & Biological Psychiatry (2002), 26(4), 677-681
CODEN: PNPPD7; ISSN: 0278-5846
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The excretion of sulfatoxymelatonin (aMT6S), a major metabolite of melatonin in urine, is dependent on noradrenergic (NA) neuronal activity within the pineal gland and thus represents a neuroendocrine marker of NA neuronal function. Many of the clin. features of opiate withdrawal result from increased firing of central NA neurons. In this study, we test the hypothesis that aMT6S excretion is increased during opiate withdrawal in opiate-dependent patients. The 24-h urinary aMT6S excretion was measured at three time points during in-patient methadone detoxification treatment in 11 opiate-dependent patients, during methadone stabilization and on Days 6 and 12 of withdrawal treatment. There was a significant increase in aMT6S excretion on Day 6 but not on Day 12, compared to stabilization. A significant correlation between individual withdrawal symptom score severity and aMT6S excretion was demonstrated during stabilization ($r=.68$, $P<.05$) and on Day 6 of treatment ($r=.62$, $P<.05$). Our preliminary findings suggest that melatonin secretion may represent a neuroendocrine marker of NA neuronal hyperactivity during opiate withdrawal in opiate-dependent patients. Areas of future research are discussed.

CC 1-2 (Pharmacology)

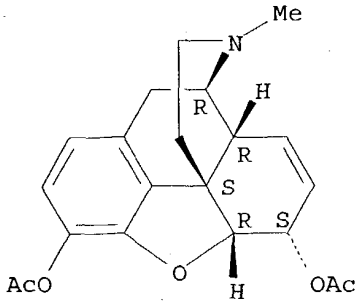
IT **Opioids**
RL: ADV (Adverse effect, including toxicity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(sulfatoxymelatonin excretion during opiate withdrawal as a **neuroendocrine** marker of noradrenergic **neuronal** hyperactivity)

IT **561-27-3**, Heroin
RL: ADV (Adverse effect, including toxicity); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(withdrawal; sulfatoxymelatonin excretion during opiate withdrawal as a neuroendocrine marker of noradrenergic neuronal hyperactivity)

IT **561-27-3**, Heroin
RL: ADV (Adverse effect, including toxicity); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(withdrawal; sulfatoxymelatonin excretion during opiate withdrawal as a neuroendocrine marker of noradrenergic neuronal hyperactivity)

RN 561-27-3 HCAPLUS
CN Morphinan-3,6-diol, 7,8-didehydro-4,5-epoxy-17-methyl-, (5α,6α)-, diacetate (ester) (9CI) (CA INDEX NAME)

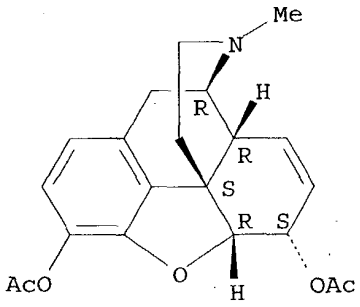
Absolute stereochemistry.



REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L29 ANSWER 12 OF 26 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:40465 HCAPLUS
DOCUMENT NUMBER: 136:241532
TITLE: Neurochemical mechanisms of heroin reinforcement
AUTHOR(S): Xi, Zheng-Xiong
CORPORATE SOURCE: Medical College of Wisconsin, Milwaukee, WI, USA
SOURCE: (2000) 141 pp. Avail.: UMI, Order No. DA3007641
From: Diss. Abstr. Int., B 2001, 62(3), 1261
DOCUMENT TYPE: Dissertation
LANGUAGE: English
AB Unavailable
CC 1-11 (Pharmacology)
Section cross-reference(s): 2
IT **Opioids**
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); BIOL (Biological study)
(**neurochem.** mechanisms of heroin reinforcement)
IT **561-27-3**, Heroin
RL: ADV (Adverse effect, including toxicity); **PAC (Pharmacological activity)**; BIOL (Biological study)
(neurochem. mechanisms of heroin reinforcement)
IT **561-27-3**, Heroin
RL: ADV (Adverse effect, including toxicity); **PAC (Pharmacological activity)**; BIOL (Biological study)
(neurochem. mechanisms of heroin reinforcement)
RN 561-27-3 HCAPLUS
CN Morphinan-3,6-diol, 7,8-didehydro-4,5-epoxy-17-methyl-(5α,6α)-, diacetate (ester) (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L29 ANSWER 13 OF 26 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:489220 HCAPLUS
DOCUMENT NUMBER: 135:97444
TITLE: Combination of trimebutine with an opioid analgesic
INVENTOR(S): Hamon, Jacques; Roman, Francois
PATENT ASSIGNEE(S): Warner-Lambert Company, USA
SOURCE: PCT Int. Appl., 63 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001047508	A2	20010705	WO 2000-EP13183	20001219
WO 2001047508	A3	20011213		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1138330	A1	20011004	EP 1999-125752	19991223
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
CA 2394745	AA	20010705	CA 2000-2394745	20001219
EP 1244498	A2	20021002	EP 2000-991630	20001219
EP 1244498	B1	20030806		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2000017035	A	20030107	BR 2000-17035	20001219
JP 2003518492	T2	20030610	JP 2001-548103	20001219
AT 246530	E	20030815	AT 2000-991630	20001219
PT 1244498	T	20031231	PT 2000-991630	20001219
ES 2202220	T3	20040401	ES 2000-991630	20001219
US 2003027835	A1	20030206	US 2001-980813	20011101
PRIORITY APPLN. INFO.:			EP 1999-125752 A	19991223
			WO 2000-EP13183 W	20001219

AB The invention provides a combination of of trimebutine [2-dimethylamino-2-phenylbutyl-3, 4, 5- trimethoxy-benzoate hydrogen maleate] or its corresponding stereoisomers with an opioid analgesic for the preparation of a medicament to prevent and/or treat pain or nociception. The antihyperalgesic activity of trimebutine in combination with morphine in prostaglandin E2-induced hyperalgesia in rats was examined

IC ICM A61K031-00
CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1
IT Nerve, disease
(**neuropathy**, treatment of; combinations of trimebutine derivs. with an opioid analgesics for treatment of pain)
IT Blood vessel
Muscle, disease
Neoplasm
Nerve

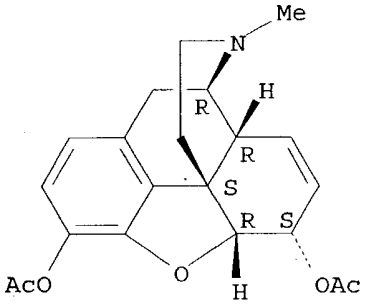
Viscera
(**pain**; combinations of trimebutine derivs. with an opioid analgesics for treatment of **pain**)

IT 57-42-1, Meperidine 76-41-5, Oxymorphone 76-57-3, Codeine 76-99-3, Methadone 77-07-6, Levorphanol 125-28-0, Dihydrocodeine 125-29-1, Hydrocodone 359-83-1, Pentazocine 437-38-7, Fentanyl 466-99-9, Hydromorphone 469-62-5, Propoxyphene **561-27-3**, Diacetylmorphine 20594-83-6, Nalbuphine 42408-82-2, Butorphanol 52485-79-7, Buprenorphine 56030-54-7 71195-58-9, Alfentanyl
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(combinations of trimebutine derivs. with an opioid analgesics for treatment of pain)

IT **561-27-3**, Diacetylmorphine
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(combinations of trimebutine derivs. with an opioid analgesics for treatment of pain)

RN 561-27-3 HCAPLUS
CN Morphinan-3,6-diol, 7,8-didehydro-4,5-epoxy-17-methyl-, (5α,6α)-, diacetate (ester) (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L29 ANSWER 14 OF 26 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:152689 HCAPLUS
DOCUMENT NUMBER: 134:188224
TITLE: Remedies for neuropathic pain and model animals of neuropathic pain
INVENTOR(S): Nagase, Hiroshi; Endo, Takashi; Kawamura, Kuniaki; Tanaka, Toshiaki; Suzuki, Tomohiko; Suzuki, Tsutomu; Kuraishi, Yasushi; Shiraki, Kimiyasu
PATENT ASSIGNEE(S): Toray Industries, Inc., Japan
SOURCE: PCT Int. Appl., 43 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001014383	A1	20010301	WO 2000-JP5690	20000824
W: CA, CN, JP, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2383146	AA	20010301	CA 2000-2383146	20000824

EP 1219624 A1 20020703 EP 2000-954975 20000824
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY
PRIORITY APPLN. INFO.: JP 1999-236778 A 19990824
WO 2000-JP5690 W 20000824
OTHER SOURCE(S): MARPAT 134:188224

AB This document discloses remedies for neuropathic pain which contain (as the active ingredients) morphinan compds. (Markush structure given) and model animals prepared by administering (+)-4a-(3-hydroxyphenyl)-2-methyl-1,2,3,4,4a,5,12,12a-octahydro-trans-quinolino[,3-g]isoquinoline. These remedies and model animals enable drug therapy for neuropathic pain and, moreover, evaluation of the therapeutic effects of compds. on neuropathic pain.

IC ICM C07D489-06
ICS C07D489-08; C07D471-04; A61K031-485; A61K031-4738; A61P025-04; A61K045-00

CC 1-11 (Pharmacology)

IT **Analgesics**
(**neuropathic** pain; morphinans as remedies for **neuropathic** pain)

IT **Opioids**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(κ-; remedies for **neuropathic** pain)

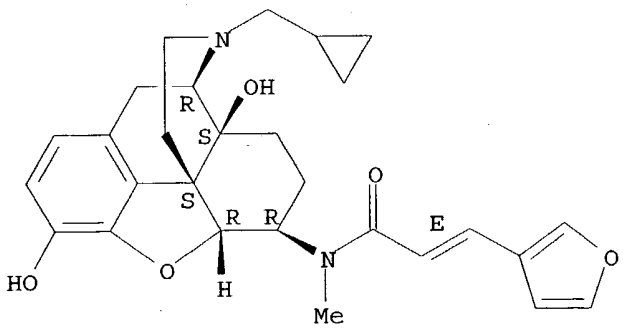
IT **152658-17-8**
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(remedy for neuropathic pain and model animals of neuropathic pain)

IT **152658-17-8**
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(remedy for neuropathic pain and model animals of neuropathic pain)

RN 152658-17-8 HCAPLUS

CN 2-Propenamide, N-[(5α,6β)-17-(cyclopropylmethyl)-4,5-epoxy-3,14-dihydroxymorphinan-6-yl]-3-(3-furanyl)-N-methyl-, monohydrochloride, (2E)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



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REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L29 ANSWER 15 OF 26 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:446228 HCAPLUS
DOCUMENT NUMBER: 133:144769
TITLE: Opiates inhibit neurogenesis in the adult rat hippocampus
AUTHOR(S): Eisch, Amelia J.; Barrot, Michel; Schad, Christina A.; Self, David W.; Nestler, Eric J.
CORPORATE SOURCE: Laboratory of Molecular Psychiatry and Yale Center for Genes and Behavior, Yale University School of Medicine, New Haven, CT, 06508, USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (2000), 97(13), 7579-7584
CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Recent work implicates regulation of neurogenesis as a form of plasticity in the adult rat hippocampus. Given the known effects of opiates such as morphine and heroin on hippocampal function, we examined opiate regulation of neurogenesis in this brain region. Chronic administration of morphine decreased neurogenesis by 42% in the adult rat hippocampal granule cell layer. A similar effect was seen in rats after chronic self-administration of heroin. Opiate regulation of neurogenesis was not mediated by changes in circulating levels of glucocorticoids, because similar effects were seen in rats that received adrenalectomy and corticosterone replacement. These findings suggest that opiate regulation of neurogenesis in the adult rat hippocampus may be one mechanism by which drug exposure influences hippocampal function.

CC 1-11 (Pharmacology)
Section cross-reference(s): 2

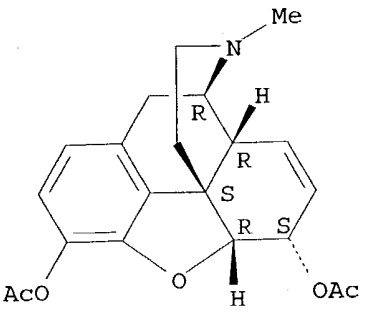
IT **Opioids**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(opiates inhibit **neurogenesis** in adult rat hippocampus)

IT 57-27-2, Morphine, biological studies **561-27-3**, Heroin
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); BIOL (Biological study)
(opiates inhibit neurogenesis in adult rat hippocampus)

IT **561-27-3**, Heroin
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); BIOL (Biological study)
(opiates inhibit neurogenesis in adult rat hippocampus)

RN 561-27-3 HCAPLUS
CN Morphinan-3,6-diol, 7,8-didehydro-4,5-epoxy-17-methyl-(5α,6α)-, diacetate (ester) (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 56 THERE ARE 56 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L29 ANSWER 16 OF 26 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:40472 HCAPLUS
DOCUMENT NUMBER: 132:189886
TITLE: Opioid modulation of hypothalamic catecholaminergic neurotransmission and the pre-ovulatory LH surge in the rat
AUTHOR(S): Yilmaz, Bayram; Gilmore, Desmond P.
CORPORATE SOURCE: Institute of Biomedical and Life Sciences, University of Glasgow, G12 8QQ, UK
SOURCE: Neuroendocrinology Letters (1999), 20(1/2), 115-121
CODEN: NLETDU; ISSN: 0172-780X
PUBLISHER: Maghira & Maas Publications
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The authors have investigated the inter-relationship between the opioid and catecholaminergic systems in the control of LH secretion, and the involvement of μ- and κ-opioid subtypes in this process. Conscious female rats were i.p. injected with either μ- (diamorphine) or κ-opioid agonists (U-50488H) alone or with their resp. antagonists (naloxone and MR2266) before the critical period on pro-estrus. Hypothalamic catecholamine and plasma LH levels were determined by HPLC-ECD and RIA, resp. Both μ- and κ-agonists significantly decreased concns. of noradrenaline and its metabolite (DHPG) in all the hypothalamic regions examined concomitant with inhibition of the LH surge. Dopamine levels were selectively reduced only by the μ-agonist in the MPOA. The inhibitory effects of both opioid agonists were mostly reversed following their co-administration with naloxone and MR2266 (except the κ-antagonist on LH). These results indicate that both the μ- and κ-opioid subtypes may be involved in the inhibition of the LH surge by altering the hypothalamic noradrenaline content.

CC 2-5 (Mammalian Hormones)

IT **Opioids**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(endogenous; opioid modulation of hypothalamic catecholaminergic **neurotransmission** and preovulatory LH surge in rat)

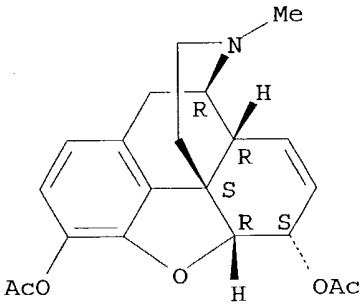
IT **561-27-3**, Diamorphine 83913-06-8, U-50488H
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(opioid modulation of hypothalamic catecholaminergic neurotransmission and preovulatory LH surge in rat)

IT **561-27-3**, Diamorphine

RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(opioid modulation of hypothalamic catecholaminergic neurotransmission and preovulatory LH surge in rat)

RN 561-27-3 HCAPLUS
CN Morphinan-3,6-diol, 7,8-didehydro-4,5-epoxy-17-methyl-, (5α,6α)-, diacetate (ester) (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L29 ANSWER 17 OF 26 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:379823 HCAPLUS
DOCUMENT NUMBER: 131:165518
TITLE: Effects of mu, kappa, and delta opioid receptor agonists and antagonists on rat hypothalamic noradrenergic neurotransmission
AUTHOR(S): Yilmaz, B.; Gilmore, D. P.
CORPORATE SOURCE: Institute of Biomedical and Life Sciences, University of Glasgow, Glasgow, UK
SOURCE: Brain Research Bulletin (1999), 48(5), 491-495
CODEN: BRBUDU; ISSN: 0361-9230
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The authors have investigated the effects of specific μ-, κ- and δ-opioid receptor agonists and antagonists on the hypothalamic noradrenergic neurotransmission and on LH (LH) release in the ovariectomized and steroid-primed rat. The opioid agents were infused intracerebroventricularly under ketamine anesthesia and blood samples collected at hourly intervals on the afternoon of the anticipated LH surge. At the end of the experiment, the rats were decapitated and the medial preoptic area, suprachiasmatic nucleus, median eminence and arcuate nucleus surgically isolated by micropunch. The concns. of noradrenaline (NA) and its metabolite (3,4-dihydroxyphenylglycol; DHPG) in these samples was determined by HPLC with electrochem. detection. Plasma LH levels were measured by RIA. The three opioid agonists reduced concns. of NA and DHPG in all four hypothalamic areas. These inhibitory effects of the opioid agonists were mostly prevented following coadministration with their resp. antagonists. However, naloxone had no significant effect on DHPG levels in any of the hypothalamic regions examined Plasma LH levels were found to be either low or undetectable in all groups. These results suggest that μ-, κ- and δ-opioid receptors have inhibitory influence on

the hypothalamic noradrenergic neurotransmission around the time of the LH surge. It is thought that the ketamine anesthesia interfered with LH release.

CC 2-5 (Mammalian Hormones)
Section cross-reference(s): 1

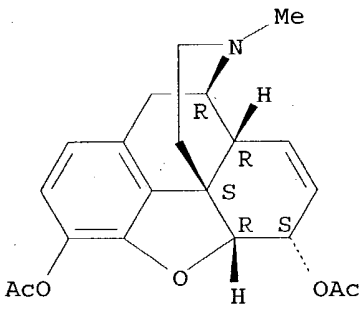
IT **Opioids**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(influence of mu, kappa, and delta opioid receptors on rat hypothalamic noradrenergic **neurotransmission** around time of LH surge)

IT 465-65-6, Naloxone **561-27-3**, Diamorphine 56649-73-1, MR1452 83420-94-4, ICI 154129 **88373-73-3** 96744-75-1, U-69593
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); BIOL (Biological study)
(influence of mu, kappa, and delta opioid receptors on rat hypothalamic noradrenergic **neurotransmission** around time of LH surge)

IT **561-27-3**, Diamorphine **88373-73-3**
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); BIOL (Biological study)
(influence of mu, kappa, and delta opioid receptors on rat hypothalamic noradrenergic **neurotransmission** around time of LH surge)

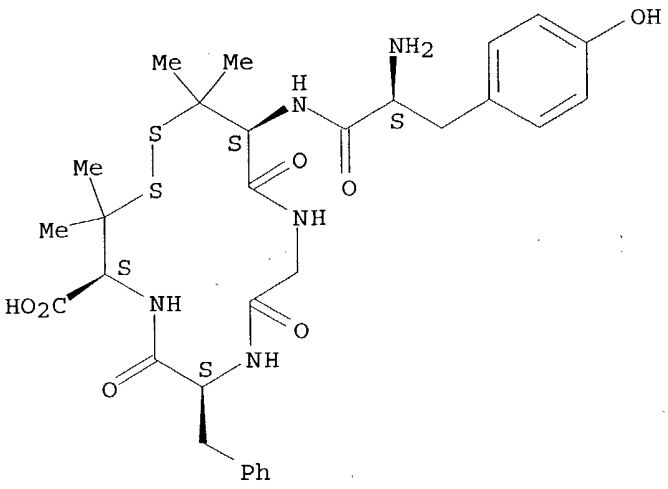
RN 561-27-3 HCAPLUS
CN Morphinan-3,6-diol, 7,8-didehydro-4,5-epoxy-17-methyl-, (5α,6α)-, diacetate (ester) (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 88373-73-3 HCAPLUS
CN D-Valine, L-tyrosyl-3-mercapto-D-valylglycyl-L-phenylalanyl-3-mercapto-, cyclic (2→5)-disulfide (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L29 ANSWER 18 OF 26 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:276351 HCAPLUS
DOCUMENT NUMBER: 131:97870
TITLE: Mu and kappa opioid modulation of the hypothalamic serotonergic neurotransmission in the ovariectomized and steroid-primed rat
AUTHOR(S): Yilmaz, B.; Gilmore, D. P.
CORPORATE SOURCE: Institute of Biomedical and Life Sciences, University of Glasgow, Glasgow, G12 8QQ, UK
SOURCE: Medical Science Research (1999), 27(2), 91-94
CODEN: MSCREJ; ISSN: 0269-8951
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English

AB We have investigated the effects of μ- and κ-opioid agonists on hypothalamic indolamine concns. and LH release in the ovariectomized and steroid-primed rat. The opioid agents and sterile saline were intracerebroventricularly infused under ketamine anesthesia and blood samples collected at hourly intervals on the afternoon of the anticipated LH surge. At the end, the rats were decapitated and the medial preoptic area (MPOA), suprachiasmatic nucleus (SCN), median eminence (ME) and arcuate nucleus (ARN) surgically isolated by micropunch. The indolamine content in these samples was determined by high performance liquid chromatog. with an electrochem. detector. Plasma LH levels were measured by RIA. Both diamorphine (μ-agonist) and U-69593 (κ-agonist) significantly reduced 5-HT concns. in all the hypothalamic regions examined 5-HIAA levels were decreased by the κ-agonist in the MPOA, SCN and ME and by the μ-agonist in only the MPOA. Plasma LH levels were either low or undetectable in all groups. These results suggest that activation of μ- and κ-opioid receptors inhibits the hypothalamic serotonergic neurotransmission around the time of the LH surge. It is thought that the ketamine anesthesia interfered with LH secretory systems.

CC 2-8 (Mammalian Hormones)
Section cross-reference(s): 1

IT **Opioids**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)

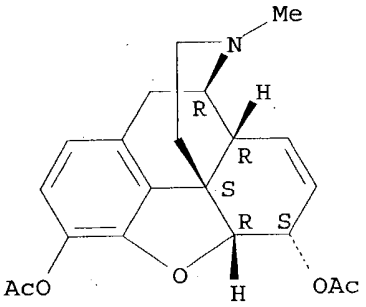
(μ- and κ-opioid modulation of hypothalamic serotonergic **neurotransmission** in ovariectomized and steroid-primed rat)

IT **561-27-3**, Diamorphine 96744-75-1, U-69593
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); BIOL (Biological study)
(μ- and κ-opioid modulation of hypothalamic serotonergic neurotransmission in ovariectomized and steroid-primed rat)

IT **561-27-3**, Diamorphine
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); BIOL (Biological study)
(μ- and κ-opioid modulation of hypothalamic serotonergic neurotransmission in ovariectomized and steroid-primed rat)

RN 561-27-3 HCAPLUS
CN Morphinan-3,6-diol, 7,8-didehydro-4,5-epoxy-17-methyl-, (5α,6α)-, diacetate (ester) (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L29 ANSWER 19 OF 26 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:126827 HCAPLUS
DOCUMENT NUMBER: 130:191898
TITLE: Substance P inhibitors in combination with NMDA blockers for treating pain
INVENTOR(S): Caruso, Frank S.
PATENT ASSIGNEE(S): Algos Pharmaceutical Corporation, USA
SOURCE: PCT Int. Appl., 54 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9907413	A1	19990218	WO 1998-US10707	19980526

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

AU 9876960 A1 19990301 AU 1998-76960 19980526
PRIORITY APPLN. INFO.: US 1997-55233P P 19970811
WO 1998-US10707 W 19980526

AB The analgesic effectiveness of a substance P receptor antagonist is significantly potentiated by administering a substance P receptor antagonist with a nontoxic NMDA receptor antagonist and/or a nontoxic substance that blocks at least one major intracellular consequence of NMDA receptor activation.

IC ICM A61K045-06
ICS A61K031-485; A61K038-04; A61K031-13; A61K038-04; A61K031-485

CC 1-11 (Pharmacology)
Section cross-reference(s): 63

IT **Pain**
(musculoskeletal or **neuropathic**; substance P inhibitor-NMDA blocker combination for treating pain)

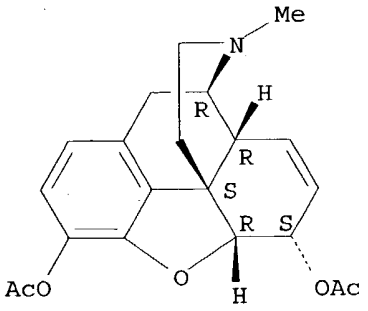
IT **Muscle, disease**
Muscle, disease
(**pain**; substance P inhibitor-NMDA blocker combination for treating **pain**)

IT 50-33-9, Phenylbutazone, biological studies 50-78-2, Aspirin 53-86-1, Indomethacin 57-27-2, Morphine, biological studies 61-68-7, Mefenamic acid 76-42-6, Oxycodone 76-57-3, Codeine 77-07-6, Levorphanol 103-90-2, Acetaminophen 125-28-0, Dihydrocodeine 125-29-1, Hydrocodone **561-27-3**, Heroin 644-62-2, Meclofenamic acid 5104-49-4, Flurbiprofen 15307-86-5, Diclofenac 15687-27-1, Ibuprofen 21256-18-8, Oxaprozin 22071-15-4, Ketoprofen 22204-53-1, Naproxen 22494-27-5, Flufenisal 22494-42-4, Diflunisal 26171-23-3, Tolmetin 27203-92-5, Tramadol 29679-58-1, Fenoprofen 33369-31-2, Zomepirac 36322-90-4 36330-85-5, Fenbufen 38194-50-2, Sulindac 41340-25-4, Etodolac 42924-53-8, Nabumetone 74103-06-3, Ketorolac
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(substance P inhibitor-NMDA blocker combination and (non)narcotic analgesics for treating pain)

IT **561-27-3**, Heroin
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(substance P inhibitor-NMDA blocker combination and (non)narcotic analgesics for treating pain)

RN 561-27-3 HCAPLUS
CN Morphinan-3,6-diol, 7,8-didehydro-4,5-epoxy-17-methyl-(5α,6α)-, diacetate (ester) (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L29 ANSWER 20 OF 26 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:579452 HCAPLUS
DOCUMENT NUMBER: 129:325982
TITLE: Anti-allodynic actions of intravenous opioids in the nerve injured rat: potential utility of heroin and dihydroetorphine against neuropathic pain
AUTHOR(S): Martin, Thomas J.; Hairston, C. Todd; Lutz, Peter O.; Harris, Louis S.; Porreca, Frank
CORPORATE SOURCE: Department of Physiology and Pharmacology, Wake Forest University School of Medicine, Winston-Salem, NC, 27157-1083, USA
SOURCE: European Journal of Pharmacology (1998), 357(1), 25-32
CODEN: EJPHAZ; ISSN: 0014-2999
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Neuropathic pain has been suggested to be resistant to treatment with opiates. Such perceived lack of opioid responsiveness may be due to the dose-range over which specific opioid compds. have been studied as well as the efficacy of these compds. Dihydroetorphine is a novel opiate that demonstrates significantly greater analgesic potency compared to morphine, and which also demonstrates diminished capacity for producing phys. dependence in laboratory animals. The present study compared the i.v. (i.v.) efficacy, potency and duration of action of dihydroetorphine, fentanyl, heroin and morphine in producing anti-allodynic actions in a rat model of neuropathic pain (ligation of the L5/L6 nerve roots). All compds. produced significant anti-allodynic activity with dihydroetorphine being the most potent (A50 of 0.2 μg kg-1, i.v.). Morphine was approx. 7440 times less potent than dihydroetorphine while heroin and fentanyl were approx. 163.5 and 6.9 times less potent in producing anti-allodynic actions. Dihydroetorphine also showed a maximal effect at 0.6 μg kg-1 in all animals tested, while 100 μg kg-1 was required for heroin to produce a maximal effect. Fentanyl and morphine did not elicit a maximum anti-allodynic response (74 and 76%maximum possible effect (%MPE), resp.). As expected, fentanyl showed a relatively brief duration of action (approx. 20 min at the highest tested dose), while dihydroetorphine and morphine demonstrated anti-allodynic actions for up to 45 min. Heroin had the longest duration of action, producing significant anti-allodynic effects for up to 90 min. These data show that dihydroetorphine and heroin produce potent and long-lasting anti-allodynic actions in this model. Addnl., in contrast to morphine and fentanyl, both dihydroetorphine and heroin were able to achieve a maximal response. The remarkable potency, maximal efficacy and duration of action of these compds., particularly dihydroetorphine, suggests that these compds. may warrant further examination as potential therapeutic treatments for neuropathic pain states.

CC 1-11 (Pharmacology)

IT **Analgesics**
(antiallodynic actions of opioids in **neuropathic** pain)

IT **Opioids**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antiallodynic actions of opioids in **neuropathic** pain)

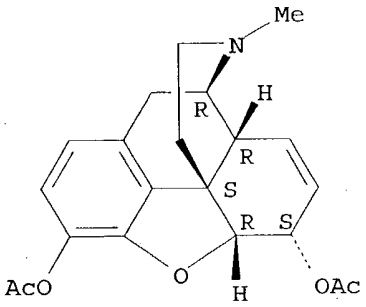
IT 57-27-2, Morphine, biological studies 437-38-7, Fentanyl **561-27-3**, Heroin 14357-76-7, Dihydroetorphine

RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(antiallodynic actions of opioids in neuropathic pain)

IT **561-27-3**, Heroin
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(antiallodynic actions of opioids in neuropathic pain)

RN 561-27-3 HCAPLUS
CN Morphinan-3,6-diol, 7,8-didehydro-4,5-epoxy-17-methyl-, (5α,6α)-, diacetate (ester) (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L29 ANSWER 21 OF 26 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1997:428193 HCAPLUS
DOCUMENT NUMBER: 127:90006
TITLE: A critique of fixed and progressive ratio schedules used to examine the neural substrates of drug reinforcement
AUTHOR(S): Arnold, Jennifer M.; Roberts, David C. S.
CORPORATE SOURCE: Institute of Neuroscience, Carleton University, Ottawa, ON, K1S 5B6, Can.
SOURCE: Pharmacology, Biochemistry and Behavior (1997), 57(3), 441-447
CODEN: PBBHAU; ISSN: 0091-3057
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with 70 refs. This paper is a critique of fixed and progressive ratio schedules used to examine the neural substrates of cocaine reinforcement. The discussion focuses on problems encountered while examining the effects of neurotoxic lesions and pharmacol. pretreatments on cocaine reinforcement. The theor. and interpretational problems associated with the use of the fixed ratio (FR) schedules that have been used in the majority of studies are discussed, and it is concluded that the rate of drug intake cannot directly address the issue of increased or decreased reinforcer efficacy. The progressive ratio schedule offers some advantages over FR schedules, although it is now clear that the same implementation cannot be applied across all drug classes. It is likely that the motivation to self-administer psychostimulant vs. opiate drugs is qual. different. It is concluded that there is no single schedule that

can quantify all aspects of drug reinforcement and that behavioral paradigms will need to be adapted according to the particular question under study.

CC 1-0 (Pharmacology)

IT **Opioids**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(fixed and progressive ratio schedules used to examine the **neural** substrates of reinforcement behavior from)

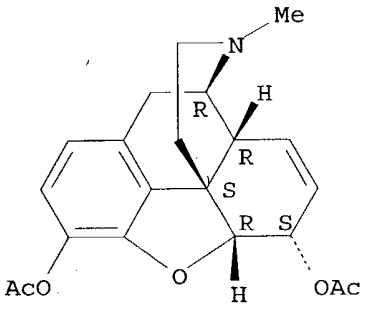
IT 50-36-2, Cocaine **561-27-3**, Heroin
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); BIOL (Biological study)
(fixed and progressive ratio schedules used to examine the neural substrates of reinforcement behavior from)

IT **561-27-3**, Heroin
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); BIOL (Biological study)
(fixed and progressive ratio schedules used to examine the neural substrates of reinforcement behavior from)

RN 561-27-3 HCAPLUS

CN Morphinan-3,6-diol, 7,8-didehydro-4,5-epoxy-17-methyl-, (5α,6α)-, diacetate (ester) (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L29 ANSWER 22 OF 26 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1996:692753 HCAPLUS

DOCUMENT NUMBER: 126:26669

TITLE: Etorphine elicits anomalous excitatory opioid effects on sensory neurons treated with GM1 ganglioside or pertussis toxin in contrast to its potent inhibitory effects on naive or chronic morphine-treated cells

AUTHOR(S): Crain, Stanley M.; Shen, Ke-Fei

CORPORATE SOURCE: Department of Neuroscience, Albert Einstein College of Medicine, Yeshiva University, 1300 Morris Park Ave, Bronx, NY, 10461, USA

SOURCE: Brain Research (1996), 741(1,2), 275-283
CODEN: BRREAP; ISSN: 0006-8993

PUBLISHER: Elsevier

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The ultra-potent opioid analgesic, etorphine, elicits naloxone-reversible, dose-dependent inhibitory effects, i.e., shortening of the action potential duration (APD) of naive and chronic morphine-treated sensory dorsal root ganglion (DRG) neurons, even at low (pM-nM) concns. In

contrast, morphine and most other opioid agonists elicit excitatory effects, i.e., APD prolongation, at these low opioid concns., require much higher (ca. 0.1-1 μM) concns. to shorten the APD of naive neurons, and evoke only excitatory effects on chronic morphine-treated cells even at high >1-10 μM concns. In addition to the potent agonist action of etorphine at μ-, δ- and κ-inhibitory opioid receptors in vivo and on DRG neurons in culture, this opioid has also been shown to be a potent antagonist of excitatory μ-, δ- and κ-receptor functions in naive and chronic morphine-treated DRG neurons. The present study demonstrates that the potent inhibitory APD-shortening effects of etorphine still occur in DRG neurons tested in the presence of a mixture of selective antagonists that blocks all μ-, δ- and κ-opioid receptor-mediated functions, whereas addition of the epsilon (ε)-opioid-receptor antagonist, β-endorphin(1-27) prevents these effects of etorphine. Furthermore, after markedly enhancing excitatory opioid receptor functions in DRG neurons by treatment with GM1 ganglioside or pertussis toxin, etorphine shows excitatory agonist action on non-μ-/δ-/κ-opioid receptor functions in these sensory neurons, in contrast to its usual potent antagonist action on μ-, δ- and κ-excitatory receptor functions in naive and even in chronic morphine-treated cells which become supersensitive to the excitatory effects of μ-, δ- and κ-opioid agonists. This weak excitatory agonist action of etorphine on non-μ-/δ-/κ-opioid receptor functions may account for the tolerance and dependence observed after chronic treatment with extremely high doses of etorphine in vivo.

CC 1-11 (Pharmacology)

IT **Analgesics**
Drug dependence
(effects of etorphine on sensory **neurons** treated with GM1 ganglioside or pertussis toxin and on naive or chronic morphine-treated cells)

IT Opioid receptors
Opioids
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(effects of etorphine on sensory **neurons** treated with GM1 ganglioside or pertussis toxin and on naive or chronic morphine-treated cells)

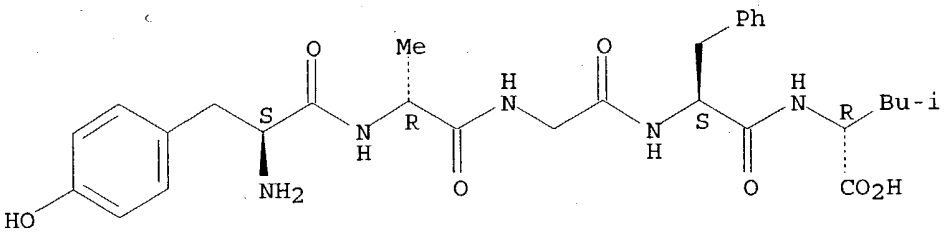
IT 57-27-2, Morphine, biological studies 14357-76-7, Dihydroetorphine 37758-47-7, GM1 ganglioside **63631-40-3 72782-05-9**, β-Funaltrexamine 72957-38-1, 1-13-Dynorphin A (swine) 76622-84-9, 1-27-β-Endorphin (human) 78123-71-4, DAGO 105618-26-6, Nor-binaltorphimine 111555-53-4, Naltrindole
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); BIOL (Biological study)
(effects of etorphine on sensory **neurons** treated with GM1 ganglioside or pertussis toxin and on naive or chronic morphine-treated cells)

IT **63631-40-3 72782-05-9**, β-Funaltrexamine
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); BIOL (Biological study)
(effects of etorphine on sensory **neurons** treated with GM1 ganglioside or pertussis toxin and on naive or chronic morphine-treated cells)

RN 63631-40-3 HCAPLUS

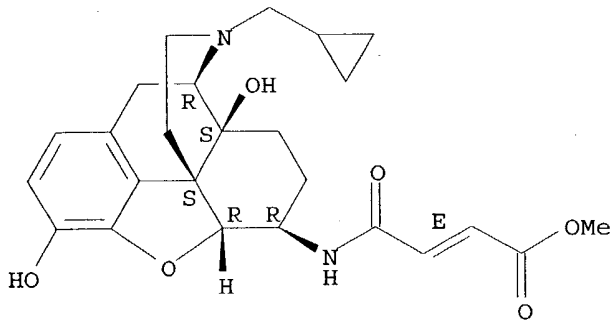
CN D-Leucine, L-tyrosyl-D-alanylglycyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 72782-05-9 HCAPLUS
CN 2-Butenoic acid, 4-[[(5α,6β)-17-(cyclopropylmethyl)-4,5-epoxy-3,14-dihydroxymorphinan-6-yl]amino]-4-oxo-, methyl ester, (2E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

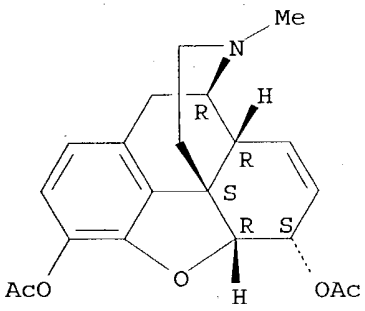


L29 ANSWER 23 OF 26 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1995:259500 HCAPLUS
DOCUMENT NUMBER: 122:24181
TITLE: Pain facilitatory systems activated by opiate receptor stimulation: possible role of NPFF, an anti-opioid peptide
AUTHOR(S): Simonnet, G.; Devillers, J.-P.; Boisserie, F.
CORPORATE SOURCE: INSERM, Bordeaux, 33077, Fr.
SOURCE: Regulatory Peptides (1994), 54(1), 277-8
CODEN: REPPDY; ISSN: 0167-0115
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The relationships between the stimulation of opiate receptors and the activation of neuropeptide FF (NPFF) system was investigated. The authors showed that: (i) the administration of naloxone (1 mg/kg) in rats 30 min following 2.5 mg/kg heroin, not only reversed analgesia, but also induced a clear hyperalgesia, as measured by tail-flick test (-30% of control); (ii) the administration of an acute dose of heroin (2.5 mg/kg) provoked a rapid (30 min) and dramatic loss (40%) of NPFF content in spinal cord; (iii) morphine induced a bell-shaped dose-dependent release of NPFF from in vitro superfused rat spinal cord slices. Thus, stimulation of opiate receptors may concomitantly activate pain inhibitory and pain facilitatory systems in which antiopioid peptides such as NPFF play a marked role. If such mechanisms were involved in tolerance, opponent processes are always present and mask, at least partly, the analgesic effects of morphine or

heroin even from first administration.
CC 2-5 (Mammalian Hormones)
Section cross-reference(s): 1
IT Analgesia
Drug tolerance
Pain
(opioid receptor stimulation activation of analgesia and pain facilitatory systems involving **neuropeptide** FF in relation to tolerance)
IT 57-27-2, Morphine, biological studies **561-27-3**, Heroin
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); BIOL (Biological study)
(opioid receptor stimulation activation of analgesia and pain facilitatory systems involving neuropeptide FF in relation to tolerance)
IT **561-27-3**, Heroin
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); BIOL (Biological study)
(opioid receptor stimulation activation of analgesia and pain facilitatory systems involving neuropeptide FF in relation to tolerance)
RN 561-27-3 HCAPLUS
CN Morphinan-3,6-diol, 7,8-didehydro-4,5-epoxy-17-methyl-(5α,6α)-, diacetate (ester) (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L29 ANSWER 24 OF 26 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1989:629907 HCAPLUS
DOCUMENT NUMBER: 111:229907
TITLE: Endogenous opioid systems regulate growth of neural tumor cells in culture [Erratum to document cited in CA111(13):112927z]
AUTHOR(S): Zagon, Ian S.; McLaughlin, Patricia J.
CORPORATE SOURCE: M. S. Hershey Med. Cent., Pennsylvania State Univ., Hershey, PA, 17033, USA
SOURCE: Brain Research (1989), 498(2), 405
CODEN: BRREAP; ISSN: 0006-8993
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Corrected Tables I and II have been provided. The errors were not reflected in the abstract or the index entries.
CC 14-1 (Mammalian Pathological Biochemistry)
Section cross-reference(s): 2
IT **Opiates and Opioids**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(**neural** cancer cell proliferation response to, structure in relation to (Erratum))

IT **Opiates and Opioids**
RL: BIOL (Biological study)
(endogenous, in **neural** cancer cell proliferation regulation, of humans and laboratory animals (Erratum))

IT **58569-55-4**
RL: PROC (Process)
(in **neural** cancer cell proliferation regulation, autocrine mechanism of, of humans and laboratory animals (Erratum))

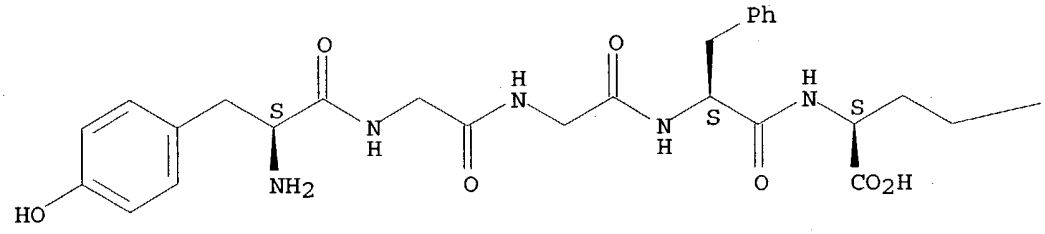
IT 52-86-8 57-27-2, biological studies 71-82-9 76-57-3 76-99-3 77-07-6 113-79-1 125-73-5 465-65-6 **561-27-3** 673-08-5 1477-40-3 14198-28-8 21778-69-8 36292-66-7 37213-49-3, α-Melanotropin 51110-01-1, Somatostatin **58822-25-6** 60117-17-1 60254-82-2 60283-51-4 61037-79-4 61090-95-7 61370-88-5 **63631-40-3** 64963-09-3 65700-73-4 67198-13-4 70904-56-2 72122-63-5 **72782-05-9** 72957-38-1 73024-95-0 75106-70-6 75513-71-2 75718-92-2, Peptide F (ox adrenal medulla) 75909-25-0 77101-32-7 78123-71-4 80501-44-6 83335-41-5, Dynorphin B (pig) 83339-89-3 88373-72-2 **88373-73-3** 88377-68-8, Adrenorphin (human) 89352-67-0 122342-35-2
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(**neural** cancer cell proliferation response to, structure in relation to (Erratum))

IT **58569-55-4**
RL: PROC (Process)
(in **neural** cancer cell proliferation regulation, autocrine mechanism of, of humans and laboratory animals (Erratum))

RN 58569-55-4 HCAPLUS
CN 1-5-Adrenorphin (human) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

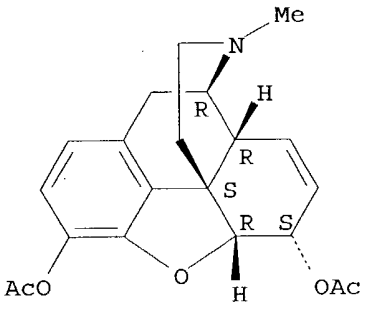
—SMe

IT **561-27-3 58822-25-6 63631-40-3 72782-05-9 88373-73-3**
RL: **BAC (Biological activity or effector, except adverse)**; BSU

(Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(**neural** cancer cell proliferation response to, structure in relation to (Erratum))

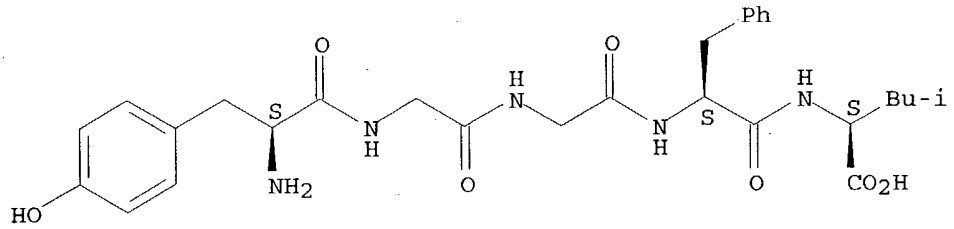
RN 561-27-3 HCAPLUS
CN Morphinan-3,6-diol, 7,8-didehydro-4,5-epoxy-17-methyl-, (5α,6α)-, diacetate (ester) (9CI) (CA INDEX NAME)

Absolute stereochemistry.



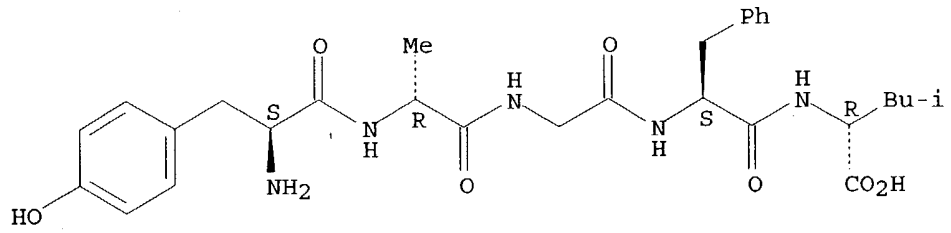
RN 58822-25-6 HCAPLUS
CN 1-5-β-Neoendorphin (human) (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 63631-40-3 HCAPLUS
CN D-Leucine, L-tyrosyl-D-alanylglycyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

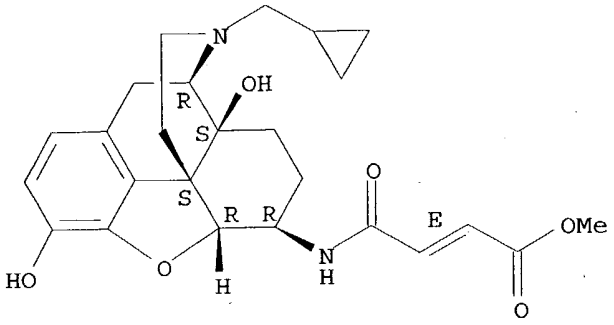
Absolute stereochemistry.



RN 72782-05-9 HCAPLUS
CN 2-Butenoic acid, 4-[[(5α,6β)-17-(cyclopropylmethyl)-4,5-epoxy-3,14-dihydroxymorphinan-6-yl]amino]-4-oxo-, methyl ester, (2E)- (9CI) (CA INDEX NAME)

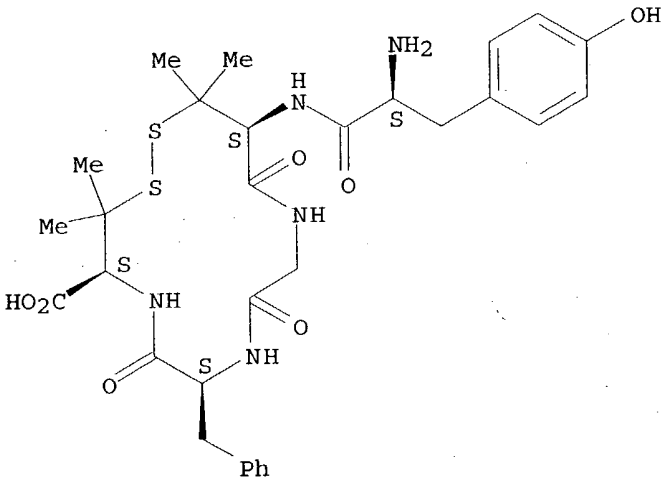
Absolute stereochemistry.

Double bond geometry as shown.



RN 88373-73-3 HCAPLUS
CN D-Valine, L-tyrosyl-3-mercapto-D-valylglycyl-L-phenylalanyl-3-mercapto-, cyclic (2→5)-disulfide (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L29 ANSWER 25 OF 26 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1989:512927 HCAPLUS
DOCUMENT NUMBER: 111:112927
TITLE: Endogenous opioid systems regulate growth of neural tumor cells in culture
AUTHOR(S): Zagon, Ian S.; McLaughlin, Patricia J.
CORPORATE SOURCE: M. S. Hershey Med. Cent., Pennsylvania State Univ., Hershey, PA, 17033, USA
SOURCE: Brain Research (1989), 490(1), 14-25
CODEN: BRREAP; ISSN: 0006-8993
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Endogenous opioid systems, i.e., opioids and opioid receptors play a role in neural cancer. By using a tissue culture system of S20Y murine neuroblastoma to assess the effects of opioids on growth, [Met5]-enkephalin was the most potent compound to influence cell replication. With a median effective concentration of 10-10 M, this peptide

inhibited cell proliferation in a stereospecific and naloxone-reversible manner. [Met5]-enkephalin depressed both DNA synthesis and mitosis. [Met5]-enkephalin was detected in neuroblastoma cells by RIA and increased in concentration in culture media over time, suggesting that these cells produced the peptide. Immunocytochem. showed [Met5]-enkephalin-like activity in the cortical cytoplasm, but not the cell nucleus, of neuroblastoma cells. Binding of [3H]-[Met5]-enkephalin was specific and saturable, and Scatchard anal. yielded a Kd of 1.2 nM and a binding capacity of 50.2 fmol/mg protein. [Met5]-enkephalin also depressed the growth of N115 murine neuroblastoma, SK-N-MC human neuroblastoma, and HT-1080 human fibrosarcoma. Thus, [Met5]-enkephalin, a naturally occurring pentapeptide that is derived from proenkephalin A, is a potent inhibitor of cell growth. Since cancer cells produce [Met5]-enkephalin, and contain a binding site to this ligand, endogenous opioid systems appear to control cell proliferation by an autocrine mechanism.

CC 14-1 (Mammalian Pathological Biochemistry)
Section cross-reference(s): 2

IT **Opiates and Opioids**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(**neural** cancer cell proliferation response to, structure in relation to)

IT **Opiates and Opioids**
RL: BIOL (Biological study)
(endogenous, in **neural** cancer cell proliferation regulation, of humans and laboratory animals)

IT **58569-55-4**, [Met5]-Enkephalin
RL: PROC (Process)
(in **neural** cancer cell proliferation regulation, autocrine mechanism of, of humans and laboratory animals)

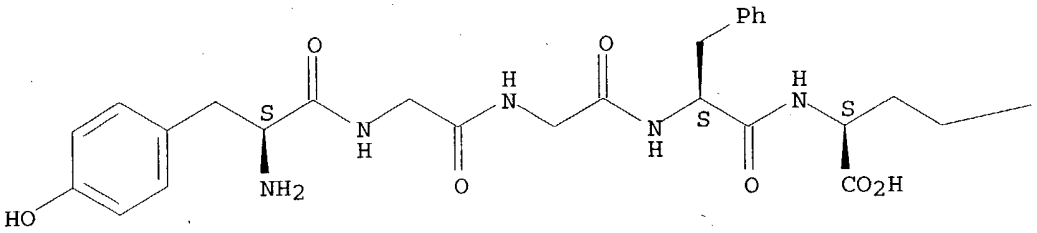
IT 52-86-8, Haloperidol 57-27-2, Morphine, biological studies 71-82-9 76-57-3, Codeine 76-99-3, Methadone 77-07-6 113-79-1, [Arg8]-Vasopressin 125-73-5, Dextrorphan 465-65-6, (-)-Naloxone **561-27-3** 673-08-5, L-Tyrosylglycine 1477-40-3 14198-28-8 21778-69-8 36292-66-7 37213-49-3, α-MSH 51110-01-1, Somatostatin **58822-25-6** 60117-17-1, [Met5]-Enkephalinamide 60254-82-2, [Des-Met5]-enkephalin 60283-51-4 61037-79-4 61090-95-7 61370-88-5 **63631-40-3** 64963-09-3 65700-73-4 67198-13-4 70904-56-2, Kyotorphin 72122-63-5 **72782-05-9**, β-Funaltrexamine 72957-38-1, Dynorphin A1-13 73024-95-0 75106-70-6 75513-71-2, BAM-12P 75718-92-2, Peptide F (ox adrenal medulla) 75909-25-0 77101-32-7, Dynorphin A1-7 78123-71-4, DAGO 80501-44-6 83335-41-5, Dynorphin B (pig) 83339-89-3 88373-72-2 **88373-73-3** 88377-68-8, Adrenorphin (human) 89352-67-0 122342-35-2
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(**neural** cancer cell proliferation response to, structure in relation to)

IT **58569-55-4**, [Met5]-Enkephalin
RL: PROC (Process)
(in **neural** cancer cell proliferation regulation, autocrine mechanism of, of humans and laboratory animals)

RN 58569-55-4 HCAPLUS
CN 1-5-Adrenorphin (human) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

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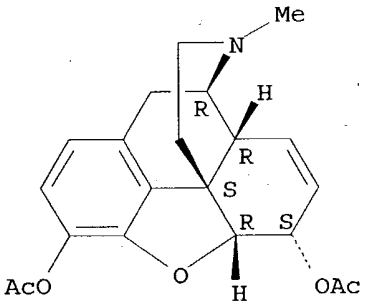
IT **561-27-3 58822-25-6 63631-40-3**
72782-05-9, β-Funaltrexamine **88373-73-3**
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(**neural** cancer cell proliferation response to, structure in relation to)

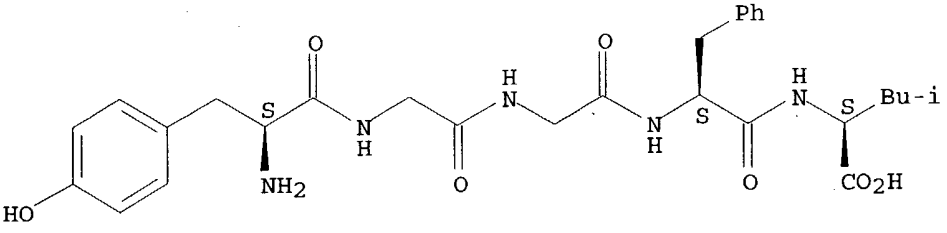
RN 561-27-3 HCAPLUS
CN Morphinan-3,6-diol, 7,8-didehydro-4,5-epoxy-17-methyl-(5α,6α)-, diacetate (ester) (9CI) (CA INDEX NAME)

Absolute stereochemistry.



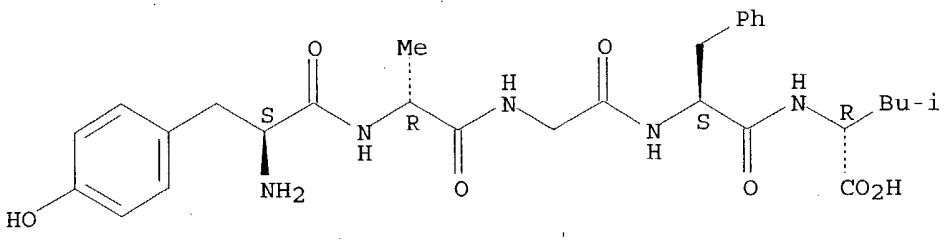
RN 58822-25-6 HCAPLUS
CN 1-5-β-Neoendorphin (human) (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



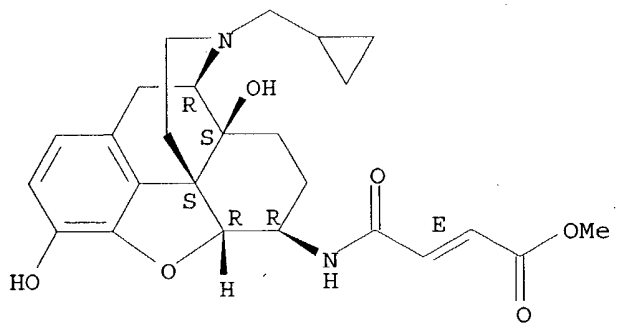
RN 63631-40-3 HCAPLUS
CN D-Leucine, L-tyrosyl-D-alanylglycyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



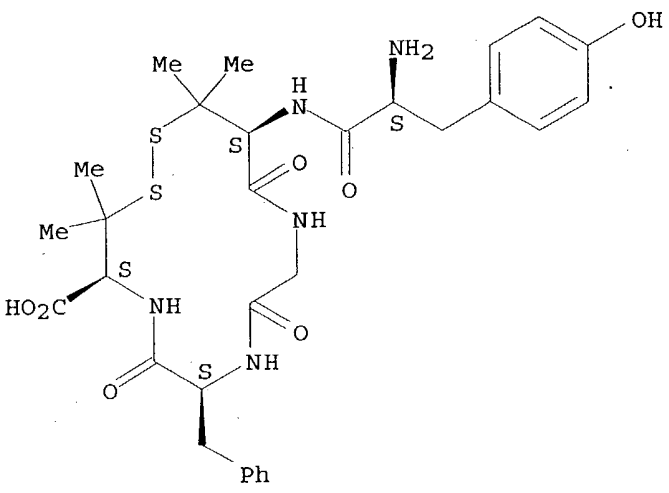
RN 72782-05-9 HCAPLUS
CN 2-Butenoic acid, 4-[[(5α,6β)-17-(cyclopropylmethyl)-4,5-epoxy-3,14-dihydroxymorphinan-6-yl]amino]-4-oxo-, methyl ester, (2E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 88373-73-3 HCAPLUS
CN D-Valine, L-tyrosyl-3-mercapto-D-valylglycyl-L-phenylalanyl-3-mercapto-, cyclic (2→5)-disulfide (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L29 ANSWER 26 OF 26 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1982:193279 HCAPLUS
DOCUMENT NUMBER: 96:193279
TITLE: Degradation of Met-enkephalin by extracts of various regions of the human brain: effects of antipsychotics and narcotics in vitro
AUTHOR(S): Jakubovic, A.
CORPORATE SOURCE: Dep. Psychiatry, Univ. British Columbia, Vancouver, BC, V6T 1W5, Can.
SOURCE: Peptides (New York, NY, United States) (1982), 3(1), 21-6
CODEN: PPTDD5; ISSN: 0196-9781
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Antischizophenic drugs reduced in a concentration-dependent fashion Met-enkephalin **[58569-55-4]** degradation by the soluble and particulate fractions of the human cerebral cortex and cerebellum. The order of potency is as follows: thioridazine [50-52-2] > chlorpromazine [50-53-3] > fluphenazine [69-23-8] > haloperidol [52-86-8] ≥ promazine [58-40-2] with IC50 of 50, 80, 120, 200-250 μM, resp. Kinetic studies revealed noncompetitive and competitive inhibition by thioridazine and chlorpromazine, resp. Narcotics were weak inhibitors of enkephalin degradation For dl- [297-88-1], d- [5653-80-5], l-methadone [125-58-6] and l-α-acetylmethadol [1477-40-3] the IC50 was about 500 μM; it was 1000 μM for heroin [561-27-3] and morphine [57-27-2]. It is suggested that inhibition of the degradation of endogenous morphinomimetic peptides in central **neurons** may be a crucial factor governing the pharmacol. of some **neuroleptics** and other psychoactive drugs. Enkephalin-hydrolyzing activity was ubiquitous and exhibited considerable regional differences in the normal human and in Huntington's chorea brains. The rate of enkephalin degradation is generally higher in the subcortical nuclei than in the cortex and cerebellum. The highest hydrolytic activity was found in the substantia nigra, anterior thalamus, septal area, globus pallidus and caudate nucleus, in decreasing order.

CC 1-11 (Pharmacology)
Section cross-reference(s): 2, 13, 14

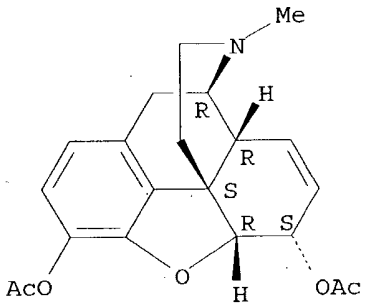
IT 50-52-2 50-53-3, biological studies 52-86-8 57-27-2, biological studies 58-40-2 69-23-8 76-99-3 125-58-6 **561-27-3** 1477-40-3 5653-80-5 58569-55-4

RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); BIOL (Biological study)
(Met-enkephalin degradation by brain response to)

IT **561-27-3**
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); BIOL (Biological study)
(Met-enkephalin degradation by brain response to)

RN 561-27-3 HCAPLUS
CN Morphinan-3,6-diol, 7,8-didehydro-4,5-epoxy-17-methyl-(5α,6α)-, diacetate (ester) (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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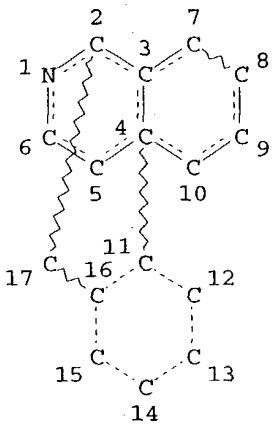

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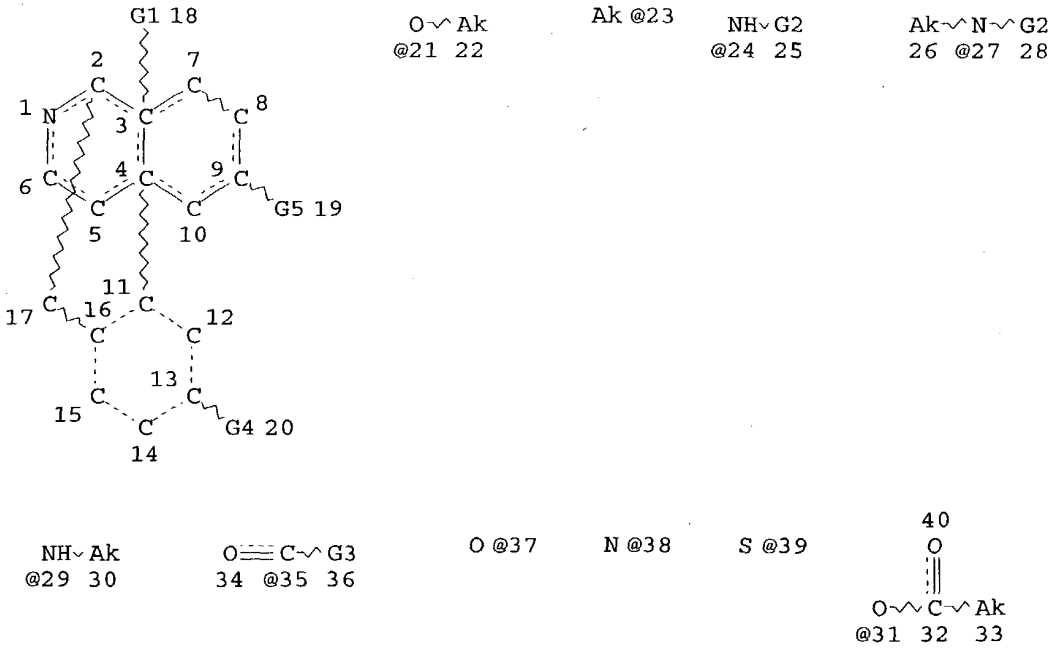

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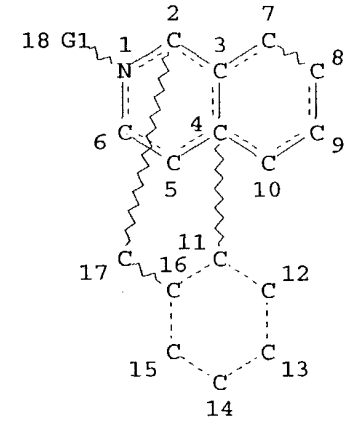

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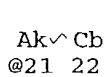

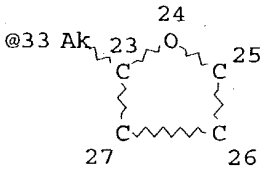

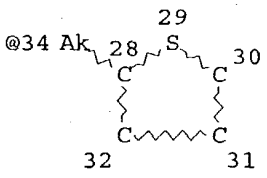

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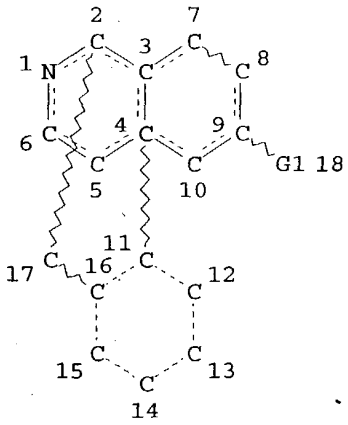

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O-G4 @45 46

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59
G3
G2-N-C-G4 19 @20 21 22

Cb @66 60 G3

N-G2 @67 68

61 G3

62 G3

63 G3

Page 1-A

O-C-G4 @23 24 25

S-C-G4 @26 27 28

G2-N-C-G3-G4 29 @30 31 32 33

O-C-G3-G4 @34 35 36 37

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Page 2-A
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VAR G3=67/O/S
VAR G4=AK/CB
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L33 ANSWER 1 OF 4 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:698121 HCAPLUS
DOCUMENT NUMBER: 141:218970
TITLE: Method and composition for potentiating an opiate analgesic
INVENTOR(S): Wang, Zaijie
PATENT ASSIGNEE(S): The Board of Trustees of the University of Illinois, USA
SOURCE: PCT Int. Appl., 74 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004071413	A2	20040826	WO 2004-US2951	20040203

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MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2004220203 A1 20041104 US 2004-769536 20040130
PRIORITY APPLN. INFO.: US 2003-446232P P 20030210

AB Composition and methods of treating pain and reducing, reversing, or preventing tolerance to opiate analgesics are disclosed. The composition and method utilize an opiate analgesic and a calcium calmodulin kinase (CaMKII) inhibitor as active agents to treat pain in mammals, including humans.

IC ICM A61K

CC 1-11 (Pharmacology)

IT Nerve, disease
(**neuropathy, pain** from; method and composition for potentiating an opiate analgesic using calcium calmodulin kinase CaMKII inhibitor in relation to preventing dependence and tolerance and treating withdrawal)

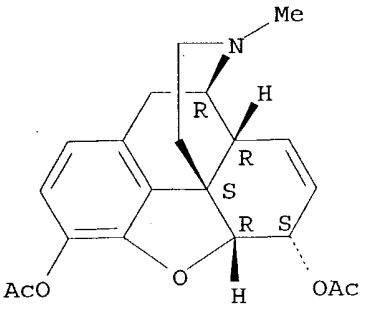
IT 50-53-3, Chlorpromazine, biological studies 52-26-6, Morphine hydrochloride 52-28-8, Codeine phosphate 57-27-2, Morphine, biological studies 57-42-1, Meperidine 59-96-1, Phenoxybenzamine 64-02-8, EDTA tetrasodium salt 64-31-3, Morphine sulfate 67-42-5, EGTA 71-68-1, Hydromorphone hydrochloride 76-57-3, Codeine 76-99-3, Methadone 117-89-5, Trifluoperazine 124-90-3, Oxycodone hydrochloride 125-69-9, Dextromethorphan hydrobromide 125-72-4, Levorphanol tartrate 140-64-7, Pentamidine isethionate 143-71-5, Hydrocodone bitartrate 302-31-8, Morphine tartrate 357-07-3, Oxymorphone hydrochloride 437-38-7, Fentanyl 466-99-9, Hydromorphone 469-62-5, Propoxyphene **561-27-3**, Diacetylmorphine 1420-53-7, Codeine sulfate **1502-95-0**, Diacetylmorphine hydrochloride 3892-78-2 4611-05-6, Ophiobolin A 16858-02-9, TPEN 35517-12-5, W-12 37231-28-0, Melittin 57265-65-3, Calmidazolium chloride 62996-74-1, Staurosporine 65595-90-6, W-7 79458-81-4, W-5 88519-57-7, W-13 91742-10-8, HA1004 99533-80-9, K-252a 103745-39-7, HA1077 115044-69-4 116826-37-0 125697-93-0, Lavendustin C 126150-97-8, BAPTA/AM 126824-24-6 127191-97-3, KN62 127243-85-0, H89 128255-42-5 139298-40-1, KN93 147504-94-7, MAPTAM 200941-84-0 201422-04-0 209329-54-4
RL: **PAC (Pharmacological activity)**; **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(method and composition for potentiating an opiate analgesic using calcium calmodulin kinase CaMKII inhibitor in relation to preventing dependence and tolerance and treating withdrawal)

IT **561-27-3**, Diacetylmorphine **1502-95-0**, Diacetylmorphine hydrochloride
RL: **PAC (Pharmacological activity)**; **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(method and composition for potentiating an opiate analgesic using calcium calmodulin kinase CaMKII inhibitor in relation to preventing dependence and tolerance and treating withdrawal)

RN 561-27-3 HCAPLUS

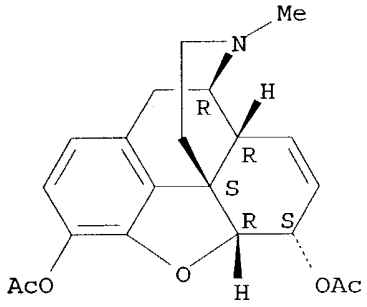
CN Morphinan-3,6-diol, 7,8-didehydro-4,5-epoxy-17-methyl-, (5α,6α)-, diacetate (ester) (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 1502-95-0 HCAPLUS
CN Morphinan-3,6-diol, 7,8-didehydro-4,5-epoxy-17-methyl-(5α,6α)-, diacetate (ester), hydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● HCl

L33 ANSWER 2 OF 4 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:757712 HCAPLUS
DOCUMENT NUMBER: 139:271069
TITLE: Methods and compositions including nitric oxide donors and opioid analgesics for pain relief
INVENTOR(S): Smith, Maree Therese; Brown, Lindsay; Harvey, Mark Bradford Pullar; Williams, Craig Mckenzie
PATENT ASSIGNEE(S): The University of Queensland, Australia
SOURCE: PCT Int. Appl., 69 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003078437	A1	20030925	WO 2003-AU335	20030320

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LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM,
PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT,
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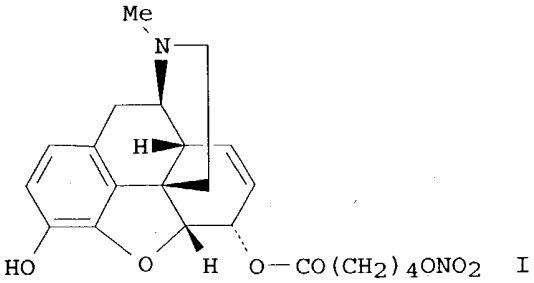
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2003219494 A1 20031127 US 2003-393050 20030320
PRIORITY APPLN. INFO.: US 2002-366594P P 20020320
OTHER SOURCE(S): MARPAT 139:271069
GI



I

AB Compns. and methods that induce, promote or otherwise facilitate pain relief are disclosed. These compns. and methods comprise a nitric oxide donor which either directly or indirectly prevents, attenuates or reverses the development of reduced opioid sensitivity, together with a compound which activates the opioid receptor that is the subject of the reduced opioid sensitivity. The compns. and methods prevent or alleviate **pain**, especially in **neuropathic** conditions and even more especially in peripheral **neuropathic** conditions such as **painful** diabetic **neuropathy**. The preferred nitric oxide donor is L-arginine, while the preferred compds. which activate the opioid receptor are morphine and oxycodone. Conjugate compds. comprising the nitric oxide donor and an opioid analgesic are also disclosed. Preparation of morphine-NO donor conjugates, e.g. I, is also described.

IC ICM C07D489-04
ICS A61K031-485; A61K031-198; A61K031-135; A61K031-4468; A61K031-454; A61K031-4535; A61P025-04

CC 1-11 (Pharmacology)
Section cross-reference(s): 31, 63

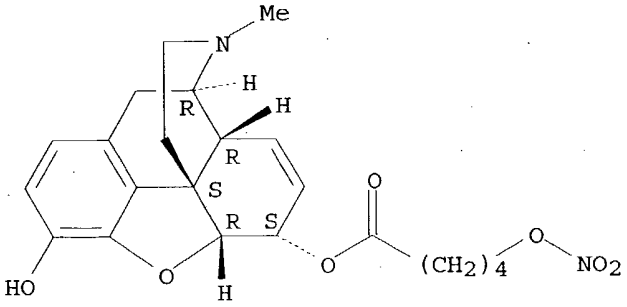
ST nitric oxide donor opioid analgesic pain treatment; arginine morphine oxycodone pain treatment; **neuropathy pain** treatment
nitric oxide donor opioid analgesic; morphine NO donor conjugate prepn pain treatment; diabetic **neuropathy pain** treatment
nitric oxide donor opioid analgesic

IT **602298-12-4P** 602298-13-5P
RL: **PAC (Pharmacological activity)**; SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(nitric oxide donors and opioid analgesics for pain relief)

IT **602298-12-4P**
RL: **PAC (Pharmacological activity)**; SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP

(Preparation); USES (Uses)
(nitric oxide donors and opioid analgesics for pain relief)
RN 602298-12-4 HCAPLUS
CN Morphinan-3,6-diol, 7,8-didehydro-4,5-epoxy-17-methyl-(5α,6α)-, 6-[5-(nitrooxy)pentanoate] (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L33 ANSWER 3 OF 4 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:240559 HCAPLUS
DOCUMENT NUMBER: 136:263477
TITLE: Preparation of dipeptide ligands of the NPFF receptor for treating pain and hyperalgesia
INVENTOR(S): Bourguignon, Jean-Jacques; Macher, Jean-Paul; Schmitt, Martine; Simmonet, Guy
PATENT ASSIGNEE(S): Institut National de la Sante et de la Recherche Medicale, Fr.; Forenap; Universite Louis Pasteur
SOURCE: PCT Int. Appl., 72 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002024192	A1	20020328	WO 2001-FR2973	20010925
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
FR 2814367	A1	20020329	FR 2000-12164	20000925
AU 2001091994	A5	20020402	AU 2001-91994	20010925
PRIORITY APPLN. INFO.:			FR 2000-12164 A	20000925
			WO 2001-FR2973 W	20010925

OTHER SOURCE(S): MARPAT 136:263477
AB The invention concerns novel compds. R4R5NCH[L-A-C(:NH)NHR12]CONR2R3 [L is (CH2)m (m = 2-4) or (CH2)nC6H4 (n = 0 or 1); A = S, NH, NMe, NPh, NCH2Ph,

where Ph may be substituted; R2, R12 = H, alkyl, aralkyl; R3 = (CH2)p-W, where p = 1, 3 or 6 and W is H, acylamino, guanidino, etc. or R2R3N may form a ring; R4 = H, Me, Ph, PhCH2, where Ph may be substituted; R5 = CO(CH2)qAr or SO2(CH2)qAr [q = 0-2; Ar = (un)substituted (hetero)aryl], or (cyclo)alkylcarbonyl], ligands of the NPFF receptor, exhibiting advantageous pharmacol. properties for treating pain. Thus, N-phenylacetyl-L-arginyl-L-phenylalaninamide diacetate was prepared by coupling of Nα-(tert-butoxycarbonyl)-Nγ-nitro-L-arginine with L-phenylalaninamide, deprotection, phenylacetylation, and hydrogenolysis.

IC ICM A61K031-198
ICS A61K038-05; A61P025-04

CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1

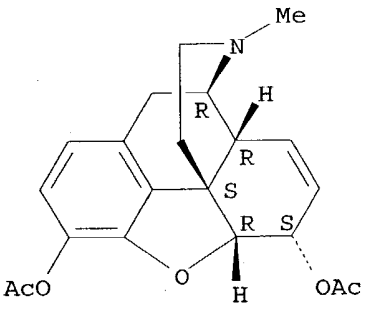
ST peptide di prepn ligand **neuropeptide** receptor **analgesic**

IT 57-27-2, Morphine, biological studies 57-42-1, Meperidine 76-99-3, Methadone 77-07-6, Levorphanol 437-38-7, Fentanyl 466-99-9, Hydromorphone **561-27-3**, Heroin 42408-82-2, Butorphanol 52485-79-7, Buprenorphine 56030-54-7, Sufentanil 71195-58-9, Alfentanyl
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(preparation of dipeptide ligands of the NPFF receptor for treating pain and hyperalgesia)

IT **561-27-3**, Heroin
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(preparation of dipeptide ligands of the NPFF receptor for treating pain and hyperalgesia)

RN 561-27-3 HCAPLUS
CN Morphinan-3,6-diol, 7,8-didehydro-4,5-epoxy-17-methyl-, (5α,6α)-, diacetate (ester) (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L33 ANSWER 4 OF 4 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:	2001:489224 HCAPLUS
DOCUMENT NUMBER:	135:97445
TITLE:	Method for relieving pain associated with an internal disease site
INVENTOR(S):	Luiken, George A.
PATENT ASSIGNEE(S):	Fluoro Probe, Inc., USA
SOURCE:	PCT Int. Appl., 31 pp. CODEN: PIXXD2
DOCUMENT TYPE:	Patent
LANGUAGE:	English

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001047512	A2	20010705	WO 2000-US42661	20001206
WO 2001047512	A3	20020502		

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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 1999-457498 A1 19991208

AB Methods are provided for in vivo administration of a pain-relieving drug, such as a local anesthetic (e.g. lidocaine), to an interior disease site for pain relief at the interior disease site. In the invention pain treatment methods, a subject is administered a targeting construct comprising a biol. compatible pain-relieving agent and a tumor-avid ligand or monoclonal antibody that preponderantly binds to or is taken up by the tissue associated with an interior disease site. Administration is by a method other than topical injection or application, such as parenteral injection. Because the pain-relieving agent is delivered by the ligand to the disease site, intractable pain situated in the interior of the body, such as is caused by various tumors, can be managed using a lower level of the pain-relieving agent then is required when the pain-relieving agent is injected in the free state.

IC ICM A61K031-00

CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1

IT Nerve, neoplasm
(**neuroblastoma**; **pain**-relieving agent-tumor avid ligand or antibody constructs for targeting internal disease site)

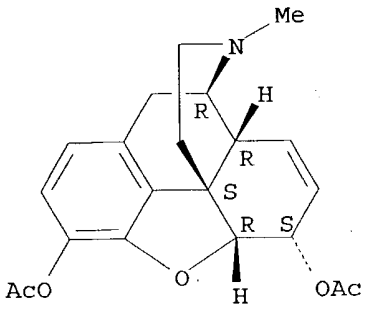
IT Endocrine system
(**neuroendocrine** system, neoplasm; **pain**-relieving agent-tumor avid ligand or antibody constructs for targeting internal disease site)

IT 57-27-2, Morphine, biological studies 57-42-1, Meperidine 59-46-1, Procaine 63-68-3, Methionine, biological studies 76-42-6, Oxycodone 76-99-3, Methadone 85-79-0, Dibucaine 94-24-6, Tetracaine 96-88-8, Mepivacaine 125-28-0, Dihydrocodeine 125-29-1, Hydrocodone 133-16-4, Chloroprocaine 136-47-0 137-58-6, Lidocaine 466-99-9, Hydromorphone 509-60-4, Dihydromorphine **561-27-3**, Heroin 721-50-6, Prilocaine 22264-50-2, 1-aminocyclobutane-1-carboxylic acid 36637-18-0, Etidocaine 38396-39-3, Bupivacaine 52485-79-7, Buprenorphine 60142-96-3, Gabapentin 66532-85-2, Propacetamol 83150-76-9, Octreotide 84057-95-4, Ropivacaine 107452-89-1, Ziconotide 108736-35-2, Lanreotide 113775-47-6, Dexmedetomidine 161982-62-3, P829 264596-75-0, P587
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(pain-relieving agent-tumor avid ligand or antibody constructs for targeting internal disease site)

IT **561-27-3**, Heroin
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(pain-relieving agent-tumor avid ligand or antibody constructs for targeting internal disease site)

RN 561-27-3 HCAPLUS
CN Morphinan-3,6-diol, 7,8-didehydro-4,5-epoxy-17-methyl-
(5α,6α)-, diacetate (ester) (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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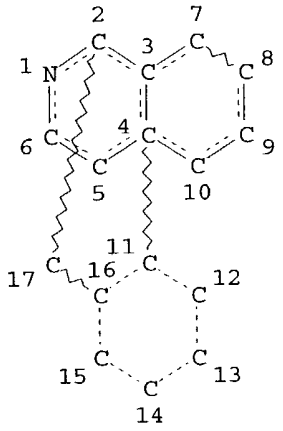

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DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
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NUMBER OF NODES IS 17

STEREO ATTRIBUTES: NONE
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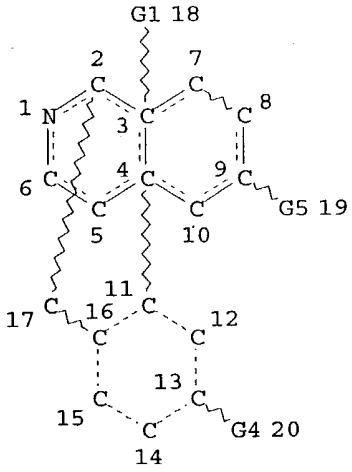

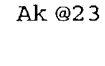

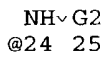

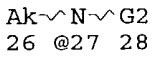

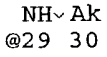

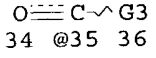

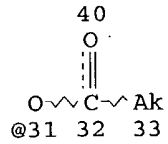

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VAR G5=37/38/39
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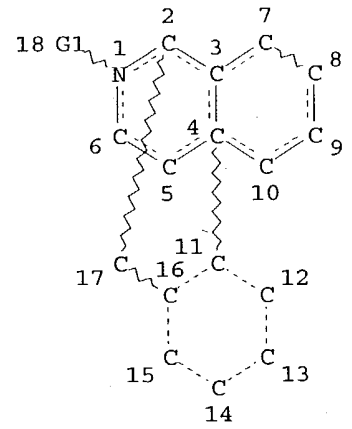
L5 STR



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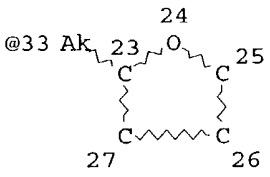

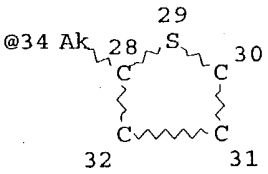

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DEFAULT ECLEVEL IS LIMITED

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NUMBER OF NODES IS 34

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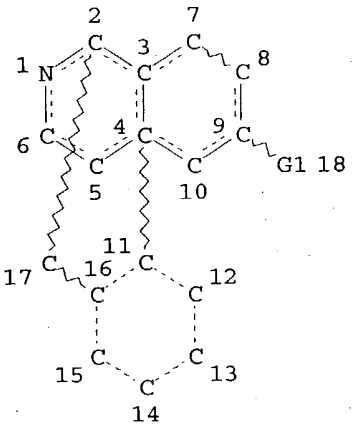

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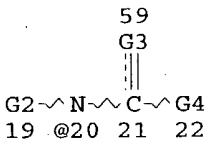
S~SO2~G4 @56 57 58



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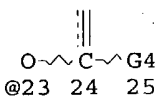
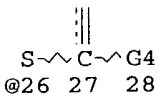
61 G3

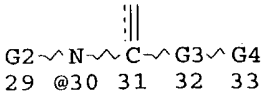
62 G3

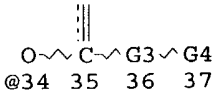
63 G3

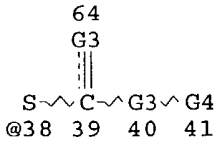
Page 1-A











Page 2-A
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VAR G2=H/65/66
VAR G3=67/O/S
VAR G4=AK/CB
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DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 68

STEREO ATTRIBUTES: NONE
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L34 468 SEA FILE=HCAPLUS ABB=ON PLU=ON "HUMAN HERPESVIRUS 3 (L) HERPES ZOSTER FROM"+OLD/CT
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L35 ANSWER 1 OF 3 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:802681 HCAPLUS
DOCUMENT NUMBER: 141:301462
TITLE: Dispersible formulations of an anti-inflammatory agent
INVENTOR(S): Britten, Nancy J.; Burns, John W.; Hallberg, John W.; Waldron, Niki A.; Watts, Jeffrey L.
PATENT ASSIGNEE(S): Pharmacia Corporation, USA
SOURCE: PCT Int. Appl., 45 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004082588	A2	20040930	WO 2004-IB826	20040310
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004235803	A1	20041125	US 2004-803146	20040317

PRIORITY APPLN. INFO.: US 2003-456325P P 20030320

AB A method is provided for treatment of an inflammatory condition in a fluid-containing organ having a natural exterior orifice, such as the udder of a milk producing animal or an ear. The method comprises administering, to the organ via the exterior orifice, a pharmaceutical composition comprising an anti-inflammatory agent and a vehicle that comprises an amphipathic oil that is water dispersible and ethanol insol., microcryst. wax and a pharmaceutically acceptable non-aqueous carrier. Also provided is such a composition comprising the anti-inflammatory agent. The composition is readily dispersible in the fluid of the fluid-containing organ. Thus, a suspension to be administered by intramammary infusion comprised parecoxib 100, Labrafil M-1944CS 50, and microcryst. wax 70 mg/mL, and cottonseed oil qs.

IC ICM A61K

CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1

IT **Human herpesvirus 3**
(**herpes zoster from**; dispersible formulations of anti-inflammatory agent)

IT Skin, disease
(**herpes**, geniculate; dispersible formulations of anti-inflammatory agent)

IT 50-02-2, Dexamethasone 50-03-3, Hydrocortisone acetate 50-23-7, Hydrocortisone 50-24-8, Prednisolone 50-33-9, Phenylbutazone, biological studies 50-78-2, Acetylsalicylic acid 52-26-6, Morphine hydrochloride 52-28-8, Codeine phosphate 53-03-2, Prednisone 53-06-5, Cortisone 53-33-8, Paramethasone 53-34-9, Fluprednisolone 53-36-1, Methylprednisolone acetate 53-86-1, Indomethacin 53-89-4, Benzpiperylon 57-08-9, ε-Acetamidocaproic acid 57-15-8, Chlorobutanol 57-27-2, Morphine, biological studies 57-42-1, Meperidine 58-15-1, Aminopyrine 60-80-0, Antipyrine 60-99-1, Methotrimeprazine 61-68-7, Mefenamic acid 62-44-2, Phenacetin 62-67-9, Nalorphine 64-31-3, Morphine sulfate 64-39-1, Promedol 64-85-7, Deoxycorticosterone 65-45-2, Salicylamide 67-73-2, Fluocinolone acetonide 68-89-3, Dipyrone 69-72-7, Salicylic acid, biological studies 76-25-5, Triamcinolone acetonide 76-41-5, Oxymorphone 76-42-6, Oxycodone 76-47-1, Hydrocortamate 76-57-3, Codeine 76-58-4, Ethylmorphine 76-99-3, Methadone 77-07-6, Levorphanol 77-14-5, Proheptazine 77-15-6, Ethoheptazine 77-20-3, Alphaprodine 83-43-2, Methylprednisolone 87-28-5, Glycol salicylate 89-45-2, Salicylsulfuric acid 89-57-6, Mesalamine 94-10-0, Ethoxazene 97-53-0, Eugenol 103-84-4, Acetanilide 103-88-8, p-Bromoacetanilide 103-90-2, Acetaminophen 103-97-9, Phenocoll 118-55-8, Phenyl salicylate 118-57-0, Acetaminosalol 124-94-7, Triamcinolone 125-27-9, Codeine methylbromide 125-28-0, Dihydrocodeine 125-29-1, Hydrocodone 127-35-5, Phenazocine 129-20-4, Oxyphenbutazone 131-28-2, Narceine 132-60-5, Cinchophen 132-89-8 134-55-4, Phenyl acetylsalicylate 136-40-3, Phenazopyridine hydrochloride 138-52-3, Salicin 143-52-2, Metopon 144-14-9, Anileridine 147-90-0, Morpholine salicylate 152-02-3, Levallorphan 152-97-6, Fluocortolone 154-82-5, Simetride 298-46-4, Carbamazepine 302-41-0, Piritramide 338-95-4, Isoflupredone 338-98-7, Isoflupredone acetate 356-12-7, Fluocinonide 357-56-2, Dextromoramide 359-83-1, Pentazocine 378-44-9, Betamethasone 382-67-2, Desoximetasone 426-13-1, Fluorometholone 427-00-9, Desomorphine 437-38-7, Fentanyl 441-61-2, Ethylmethylthiambutene 466-40-0, Isomethadone 466-90-0, Dihydrocodeinone enol acetate 466-97-7, Normorphine 466-99-9, Hydromorphone 467-18-5, Myrophine 467-83-4, Dipipanone 467-84-5, Phenadoxone 467-85-6, Normethadone 467-86-7, Dioxaphetyl butyrate 468-07-5, Phenomorphan 468-56-4, Hydroxypethidine 469-62-5, Propoxyphene 469-79-4, Ketobemidone

471-53-4, Enoxolone 479-92-5, Propyphenazone 486-79-3, Dipyrocetyl
487-48-9, Salacetamide 489-84-9, Guaiazulene 490-79-9, Gentisic acid
508-99-6, Hydrocortisone cypionate 509-60-4, Dihydromorphine 509-78-4,
Dimenoxadol 515-69-5, α-Bisabolol 518-34-3, Tetrandrine
524-84-5, Dimethylthiambutene 528-94-9, Ammonium salicylate 530-34-7,
Isoladol 530-78-9, Flufenamic acid 539-08-2, p-Lactophenetide
545-90-4, Dimepheptanol 550-97-0, 1-Naphthyl salicylate 552-25-0,
Diampromide 552-94-3, Salsalate 553-20-8, 5'-Nitro-2'-
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Benzydamine 644-62-2, Meclofenamic acid 695-34-1, 2-Amino-4-picoline
841-73-6, Bucolome 846-48-0, Dehydrotestosterone 911-65-9, Etonitazene
938-73-8, Ethenzamide 959-10-4, Xenbucin 1083-57-4, Bucetin
1110-40-3, Cortivazol 1247-42-3, Meprednisone 1420-53-7, Codeine
sulfate 1503-53-3, 5-Bromosalicylic acid acetate 1524-88-5,
Flurandrenolide 1531-12-0, Norlevorphanol 1553-60-2, Ibufenac
1729-61-9, Paranyline 2016-36-6, Choline salicylate, biological studies
2037-95-8, Carsalam 2055-44-9, Perisoxal 2109-73-1, Butacetin
2135-17-3, Flumethasone 2139-47-1, Nifenazone 2152-44-5,
Betamethasone-17-valerate 2154-02-1, Metofoline 2193-87-5,
Fluprednidene 2203-97-6, Hydrocortisone succinate 2210-63-1,
Mofebutazone 2265-64-7, Dexamethasone-21-isonicotinate 2316-64-5,
Bromosaligenin 2375-03-3, Methylprednisolone sodium succinate
2438-72-4, Bufexamac 2531-04-6, Piperylone 2557-49-5, Diflorasone
2607-06-9, Diflucortolone 2668-66-8, Medrysone 2825-60-7, Formocortal
2924-67-6, Fluoresone 3093-35-4, Halcinonide 3385-03-3, Flunisolide
3426-01-5, Phenopyrazone 3567-76-8, Aminochlorthenoxazin 3572-80-3,
Cyclazocine 3583-64-0, Bumadizon 3615-24-5, Ramifenazone 3690-04-8,
Aminopropylon 3693-39-8, Flucloronide 3734-52-9, Metazocine
3820-67-5, Glafenine 3841-11-0, Fluperolone 3861-76-5, Clonitazene
4394-00-7, Niflumic acid 4419-39-0, Beclomethasone 4741-41-7,
Dexoxadrol 4828-27-7, Clocortolone 5003-48-5, Benorylate 5104-49-4,
Flurbiprofen 5251-34-3, Cloprednol 5696-09-3, Proxazole 5728-52-9,
Felbinac 6064-83-1, Fosfosal 6168-76-9, Crotethamide 6376-26-7,
Salverine 6536-18-1, Morazone 7262-75-1, Lefetamine 9014-67-9,
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22494-42-4, Diflunisal 22760-18-5, Proquazone 23049-93-6, Enfenamic
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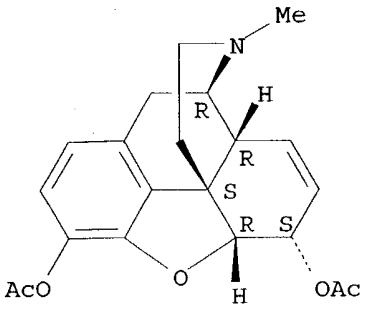
24237-54-5, Tinoridine
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(dispersible formulations of anti-inflammatory agent)

IT **561-27-3**, Diamorphine
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(dispersible formulations of anti-inflammatory agent)

RN 561-27-3 HCAPLUS

CN Morphinan-3,6-diol, 7,8-didehydro-4,5-epoxy-17-methyl-
(5α,6α)-, diacetate (ester) (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L35 ANSWER 2 OF 3 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:292543 HCAPLUS
DOCUMENT NUMBER: 140:368547
TITLE: Suppression of acute herpetic pain-related responses by the κ-opioid receptor agonist (-)-17-Cyclopropylmethyl-3,14β-dihydroxy-4,5α-epoxy-6β-[N-methyl-3-trans-3-(3-furyl) acrylamido] morphinan hydrochloride (TRK-820) in mice
AUTHOR(S): Takasaki, Ichiro; Suzuki, Tomohiko; Sasaki, Atsushi; Nakao, Kaoru; Hirakata, Mikito; Okano, Kiyoshi; Tanaka, Toshiaki; Nagase, Hiroshi; Shiraki, Kimiyasu; Nojima, Hiroshi; Kuraishi, Yasushi
CORPORATE SOURCE: Department of Applied Pharmacology, Faculty of Pharmaceutical Sciences, Toyama Medical and Pharmaceutical University, Toyama, Japan
SOURCE: Journal of Pharmacology and Experimental Therapeutics (2004), 309(1), 36-41
CODEN: JPETAB; ISSN: 0022-3565
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE: Journal
LANGUAGE: English
AB (-)-17-Cyclopropylmethyl-3,14β-dihydroxy-4,5α-epoxy-6β-[N-methyl-3-trans-3-(3-furyl) acrylamido] morphinan hydrochloride (TRK-820) is a κ-opioid receptor agonist that has pharmacol. characteristics different from typical κ-opioid receptor agonists. This study was conducted to determine the antiallodynic and antihyperalgesic effects of TRK-820 in a mouse model of acute herpetic pain and to compare them with those of the κ-opioid receptor agonist enadoline and the μ-opioid receptor agonist morphine. Percutaneous inoculation with **herpes** simplex virus type-1 induced tactile allodynia and mech. hyperalgesia in the hind paw on the inoculated side. TRK-820 (0.01 - 0.1 mg/kg p.o.), enadoline (1 - 10 mg/kg p.o.) and morphine (5 - 20 mg/kg p.o.) dose dependently inhibited the allodynia and hyperalgesia, but the antiallodynic and antihyperalgesic dose of enadoline markedly decreased spontaneous locomotor activity. The antinociceptive action of TRK-820 (0.1 mg/kg) was completely antagonized by pretreatment with norbinaltorphimine, a κ-opioid receptor antagonist, but not by naltrexone, a μ-opioid receptor antagonist. Repeated treatment with morphine (20 mg/kg, four times) resulted in the reduction of antiallodynic and

antihyperalgesic effects, whereas the inhibitory potency of TRK-820 (0.1 mg/kg) was almost the same even after the fourth administration. There was no cross-tolerance in antinociceptive activities between TRK-820 and morphine. Intrathecal and intracerebroventricular, but not intraplantar, injections of TRK-820 (10 - 100 ng/site) suppressed the allodynia and hyperalgesia. These results suggest that TRK-820 inhibits acute herpetic pain through κ-opioid receptors in the spinal and supraspinal levels. TRK-820 may have clin. efficacy in acute herpetic pain with enough safety margins.

CC 1-11 (Pharmacology)

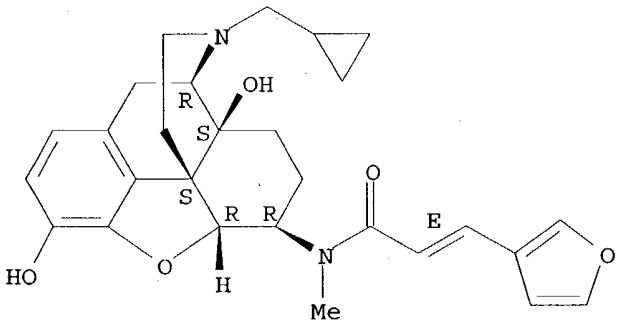
IT **152658-17-8**, TRK-820
RL: **DMA (Drug mechanism of action)**; **PAC (Pharmacological activity)**; **THU (Therapeutic use)**; BIOL (Biological study);
USES (Uses)
(suppression of acute herpetic pain-related responses by the κ-opioid receptor agonist (-)-17-Cyclopropylmethyl-3,14β-dihydroxy-4,5α-epoxy-6β-[N-Me-3-trans-3-(3-furyl) acrylamido] morphinan hydrochloride (TRK-820) in mice)

IT **152658-17-8**, TRK-820
RL: **DMA (Drug mechanism of action)**; **PAC (Pharmacological activity)**; **THU (Therapeutic use)**; BIOL (Biological study);
USES (Uses)
(suppression of acute herpetic pain-related responses by the κ-opioid receptor agonist (-)-17-Cyclopropylmethyl-3,14β-dihydroxy-4,5α-epoxy-6β-[N-Me-3-trans-3-(3-furyl) acrylamido] morphinan hydrochloride (TRK-820) in mice)

RN 152658-17-8 HCAPLUS

CN 2-Propenamide, N-[(5α,6β)-17-(cyclopropylmethyl)-4,5-epoxy-3,14-dihydroxymorphinan-6-yl]-3-(3-furanyl)-N-methyl-, monohydrochloride, (2E)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



● HCl

REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L35 ANSWER 3 OF 3 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:757712 HCAPLUS
DOCUMENT NUMBER: 139:271069
TITLE: Methods and compositions including nitric oxide donors

and opioid analgesics for pain relief

INVENTOR(S): Smith, Maree Therese; Brown, Lindsay; Harvey, Mark Bradford Pullar; Williams, Craig Mckenzie

PATENT ASSIGNEE(S): The University of Queensland, Australia

SOURCE: PCT Int. Appl., 69 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

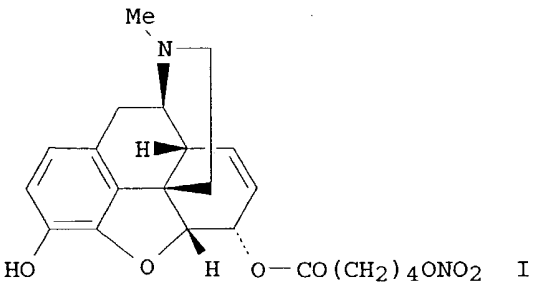
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003078437	A1	20030925	WO 2003-AU335	20030320
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003219494	A1	20031127	US 2003-393050	20030320
PRIORITY APPLN. INFO.:			US 2002-366594P P	20020320

OTHER SOURCE(S): MARPAT 139:271069

GI



I

AB Compns. and methods that induce, promote or otherwise facilitate pain relief are disclosed. These compns. and methods comprise a nitric oxide donor which either directly or indirectly prevents, attenuates or reverses the development of reduced opioid sensitivity, together with a compound which activates the opioid receptor that is the subject of the reduced opioid sensitivity. The compns. and methods prevent or alleviate pain, especially in neuropathic conditions and even more especially in peripheral neuropathic conditions such as painful diabetic neuropathy. The preferred nitric oxide donor is L-arginine, while the preferred compds. which activate the opioid receptor are morphine and oxycodone. Conjugate compds. comprising the nitric oxide donor and an opioid analgesic are also disclosed. Preparation of morphine-NO donor conjugates, e.g. I, is also described.

IC ICM C07D489-04
ICS A61K031-485; A61K031-198; A61K031-135; A61K031-4468; A61K031-454; A61K031-4535; A61P025-04

CC 1-11 (Pharmacology)
Section cross-reference(s): 31, 63

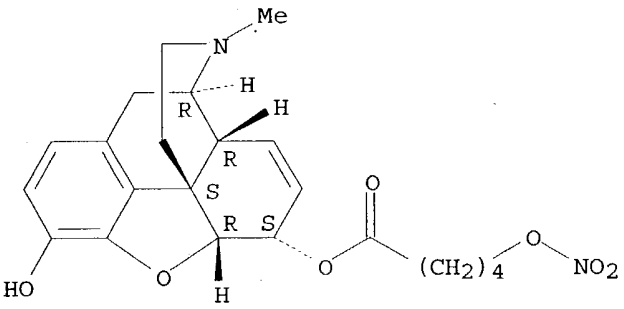
IT **Human herpesvirus 3**
(**herpes zoster from**, neuropathic
condition associated with; nitric oxide donors and opioid analgesics for
pain relief)

IT **602298-12-4P** 602298-13-5P
RL: **PAC (Pharmacological activity)**; SPN (Synthetic preparation);
THU (Therapeutic use); BIOL (Biological study); PREP
(Preparation); USES (Uses)
(nitric oxide donors and opioid analgesics for pain relief)

IT **602298-12-4P**
RL: **PAC (Pharmacological activity)**; SPN (Synthetic preparation);
THU (Therapeutic use); BIOL (Biological study); PREP
(Preparation); USES (Uses)
(nitric oxide donors and opioid analgesics for pain relief)

RN 602298-12-4 HCAPLUS
CN Morphinan-3,6-diol, 7,8-didehydro-4,5-epoxy-17-methyl-
(5α,6α)-, 6-[5-(nitrooxy)pentanoate] (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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=> dup rem l29 l33 l38
PROCESSING COMPLETED FOR L29
PROCESSING COMPLETED FOR L33
PROCESSING COMPLETED FOR L38
L39           90 DUP REM L29 L33 L38 (23 DUPLICATES REMOVED)
                 ANSWERS '1-35' FROM FILE HCAPLUS
                 ANSWERS '36-40' FROM FILE MEDLINE
                 ANSWERS '41-61' FROM FILE EMBASE
                 ANSWERS '62-65' FROM FILE BIOSIS
                 ANSWERS '66-90' FROM FILE USPATFULL

=> d que l39
L1                STR
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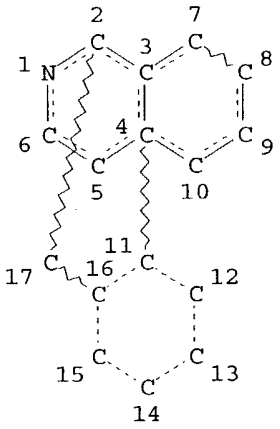


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CONNECT IS E3  RC AT   9
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DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  17

STEREO ATTRIBUTES: NONE
L2         10791 SEA FILE=REGISTRY SSS FUL L1
L3               STR
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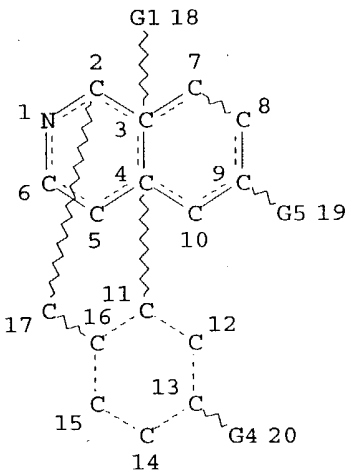


O~Ak
@21 22

Ak @23

NH~G2
@24 25

Ak~N~G2
26 @27 28

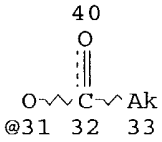
NH~Ak
@29 30

O≡C~G3
34 @35 36

O @37

N @38

S @39



VAR G1=H/OH/NO2/31/21/23/NH2/24/27/29
VAR G2=23/35
VAR G3=H/PH/23
VAR G4=H/OH/31/21
VAR G5=37/38/39
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CONNECT IS E2 RC AT 37
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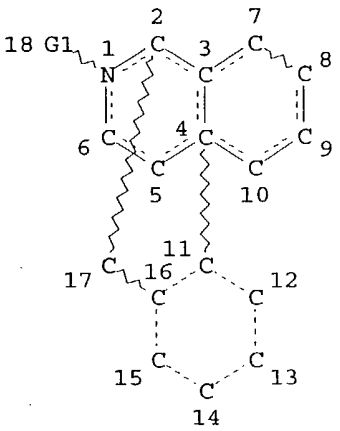
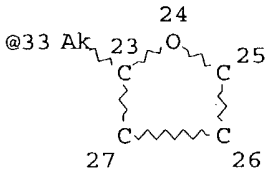
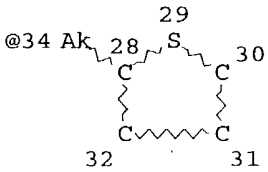
L5 STR



Ak @19 Cb @20

Ak Cb
@21 22





VAR G1=19/20/21/33/34
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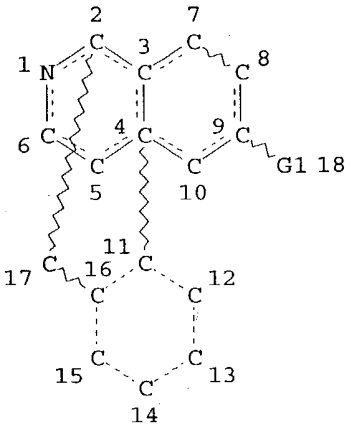
CONNECT IS E1 RC AT 20
CONNECT IS E2 RC AT 21
CONNECT IS E1 RC AT 22
CONNECT IS E2 RC AT 25
CONNECT IS E2 RC AT 26
CONNECT IS E2 RC AT 27
CONNECT IS E2 RC AT 30
CONNECT IS E2 RC AT 31
CONNECT IS E2 RC AT 32
CONNECT IS E2 RC AT 33
CONNECT IS E2 RC AT 34
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 34

STEREO ATTRIBUTES: NONE
L6 2736 SEA FILE=REGISTRY SUB=L4 SSS FUL L5
L7 STR



G2~N~G4
42 @43 44

O~G4
@45 46

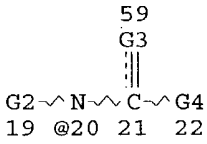
S~G4
@47 48

Ak @65

G2~N~SO2G4
49 @50 51 52

O~SO2G4
@53 54 55

S~SO2G4
@56 57 58



Cb @66
60
G3

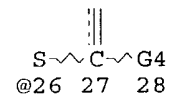
N~G2
@67 68

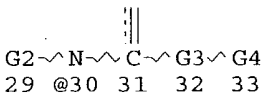
61
G3

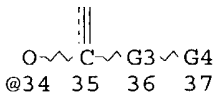
62
G3

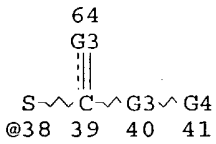
63
G3

Page 1-A









Page 2-A
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VAR G3=67/O/S
VAR G4=AK/CB
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DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
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NUMBER OF NODES IS 68

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L21          664 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L8(L)(BAC OR DMA OR PAC OR
                 PKT OR THU)/RL
L27         4434 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ANALGESICS+OLD,NT/CT(L)NEUR?
L28         3708 SEA FILE=HCAPLUS ABB=ON  PLU=ON  PAIN+NT/CT(L)NEUR?
L29           26 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L21 AND (L27 OR L28)
L31           12 SEA FILE=HCAPLUS ABB=ON  PLU=ON  NEURO?(3A)(ANALGES? OR PAIN?)
                 AND L21
L33            4 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L31 NOT L29
L38           83 SEA L8 AND (ZOSTER OR NEUROP?(3A) PAIN?)
L39           90 DUP REM L29 L33 L38 (23 DUPLICATES REMOVED)


=> d bib ab 36-90

L39  ANSWER 36 OF 90     MEDLINE on STN                  DUPLICATE 11
AN   2001404956     MEDLINE
DN   PubMed ID: 11438603
TI   Inhibition of neuropathic pain by selective ablation
     of brainstem medullary cells expressing the mu-opioid receptor.
AU   Porreca F; Burgess S E; Gardell L R; Vanderah T W; Malan T P Jr; Ossipov M
     H; Lappi D A; Lai J
CS   Departments of Pharmacology and Anesthesiology, University of Arizona,
     Tucson, Arizona 85724, USA.. frankp@u.arizona.edu
SO   Journal of neuroscience : official journal of the Society for
     Neuroscience, (2001 Jul 15) 21 (14) 5281-8.
     Journal code: 8102140. ISSN: 1529-2401.
CY   United States
DT   Journal; Article; (JOURNAL ARTICLE)
LA   English
FS   Priority Journals
EM   200107
ED   Entered STN: 20010730
     Last Updated on STN: 20021211
     Entered Medline: 20010726
AB   Neurons in the rostroventromedial medulla (RVM) project to spinal loci
     where the neurons inhibit or facilitate pain transmission.  Abnormal
     activity of facilitatory processes may thus represent a mechanism of
     chronic pain.  This possibility and the phenotype of RVM cells that might
     underlie experimental neuropathic pain were
     investigated.  Cells expressing mu-opioid receptors were targeted with a
     single microinjection of saporin conjugated to the mu-opioid agonist
     dermorphin; unconjugated saporin and dermorphin were used as controls.
     RVM dermorphin-saporin, but not dermorphin or saporin, significantly
     decreased cells expressing mu-opioid receptor transcript.  RVM dermorphin,
     saporin, or dermorphin-saporin did not change baseline hindpaw sensitivity
     to non-noxious or noxious stimuli.  Spinal nerve ligation (SNL) injury in
     rats pretreated with RVM dermorphin-saporin failed to elicit the expected
     increase in sensitivity to non-noxious mechanical or noxious thermal
     stimuli applied to the paw.  RVM dermorphin or saporin did not alter
     SNL-induced experimental pain, and no pretreatment affected the responses
     of sham-operated groups.  This protective effect of dermorphin-saporin
     against SNL-induced pain was blocked by beta-funaltrexamine, a selective
     mu-opioid receptor antagonist, indicating specific interaction of
     dermorphin-saporin with the mu-opioid receptor.  RVM microinjection of
     dermorphin-saporin, but not of dermorphin or saporin, in animals
     previously undergoing SNL showed a time-related reversal of the
```

SNL-induced experimental pain to preinjury baseline levels. Thus, loss of RVM mu receptor-expressing cells both prevents and reverses experimental **neuropathic pain**. The data support the hypothesis that inappropriate tonic-descending facilitation may underlie some chronic pain states and offer new possibilities for the design of therapeutic strategies.

L39 ANSWER 37 OF 90 MEDLINE on STN DUPLICATE 14
AN 96021386 MEDLINE
DN PubMed ID: 7595681
TI **Painful** sciatic **neuropathy** after heroin overdose.
AU Gille M; Delbecq J; Depre A; van den Bergh P
SO Journal of neurology, (1995 Jul) 242 (7) 478-80.
Journal code: 0423161. ISSN: 0340-5354.
CY GERMANY: Germany, Federal Republic of
DT (CASE REPORTS)
Letter
LA English
FS Priority Journals
EM 199512
ED Entered STN: 19960124
Last Updated on STN: 19990129
Entered Medline: 19951219

L39 ANSWER 38 OF 90 MEDLINE on STN DUPLICATE 15
AN 96192273 MEDLINE
DN PubMed ID: 8624708
TI Simultaneous activation of spinal antiopioid system (**neuropeptide** FF) and **pain** facilitatory circuitry by stimulation of opioid receptors in rats.
AU Devillers J P; Boisserie F; Laulin J P; Larcher A; Simonnet G
CS INSERM U. 259, Universite de Bordeaux II, Laboratoire de Psychobiologie des comportements adaptatifs, France.
SO Brain research, (1995 Nov 27) 700 (1-2) 173-81.
Journal code: 0045503. ISSN: 0006-8993.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199606
ED Entered STN: 19960708
Last Updated on STN: 19990129
Entered Medline: 19960624
AB Neuropeptide FF (NPFF) is a mammalian FMRFamide-like octapeptide with antiopioid properties that inhibits morphine-induced analgesia but also produces hyperalgesia. In the present study, a series of three experiments was carried out to investigate the interactions between opioid receptor stimulation and antiopioid systems. First, by using in vitro superfusion system with rat spinal cord slices, we showed that morphine stimulated NPFF release in a dose-dependent manner. The stimulating effect which was observed with morphine concentrations as low as 100 fM reached a maximum at 0.1 nM, then decreased and was ineffective at 10 microM. The morphine-induced release of NPFF was abolished by naloxone (1 microM) but unaltered by tetrodotoxin. Second, by an in vivo approach, we showed that a single heroin administration (2.5 mg/kg, s.c.) elicited in 30 min a drastic drop (38%) in spinal NPFF content. In a third experiment, we evaluated the capacity of naloxone in revealing an antiopioid component associated with opioid receptor stimulation. The administration of naloxone (1 mg/kg, s.c..) 25 min following that of

heroin (2.5 mg/kg, s.c.) not only abolished the heroin-induced increase of tail-flick latency, but also lowered it under the basal value by 30%. These results indicate that opioid receptor stimulation activates both pain inhibitory and pain facilitatory systems in which NPFF may play a significant role and that opiate-induced analgesia is always partly masked.

L39 ANSWER 39 OF 90 MEDLINE on STN DUPLICATE 16
AN 94247657 MEDLINE
DN PubMed ID: 7514771
TI Opioid responsiveness of cancer **pain** syndromes caused by **neuropathic** or nociceptive mechanisms: a combined analysis of controlled, single-dose studies.
AU Cherny N I; Thaler H T; Friedlander-Klar H; Lapin J; Foley K M; Houde R; Portenoy R K
CS Department of Neurology, Memorial Sloan-Kettering Cancer Center, New York, NY 10021.
NC CA32897 (NCI)
SO Neurology, (1994 May) 44 (5) 857-61.
Journal code: 0401060. ISSN: 0028-3878.
CY United States
DT (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(RANDOMIZED CONTROLLED TRIAL)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 199406
ED Entered STN: 19940629
Last Updated on STN: 19990129
Entered Medline: 19940620
AB We performed a combined analysis of the results from four controlled single-dose relative-potency studies to assess the impact of inferred pain mechanism on the response to an opioid drug. A total of 168 patients received 474 administrations of either morphine or heroin, and we assessed the analgesic response during a 6-hour period with visual analog scales. We summarized this as a total pain relief (TOTPAR) score. Two experienced pain clinicians reviewed information about pain characteristics and designated each case according to the inferred **pain** mechanism (**neuropathic**, nociceptive, or mixed) and the degree of confidence in the inferred mechanism (definite versus probable/possible). They grouped the cases as follows: nociceptive **pain** only (n = 205), **neuropathic pain** only (n = 49), and mixed (n = 220). We compared pain relief achieved by patients with different mechanisms, with TOTPAR adjusted for significant covariates (duration of prior opioid administration, doses of opioid administered in the previous 48 hours, pain intensity at the start of the study, BUN:creatinine ratio, and dose of administered opioid). The adjusted mean TOTPAR score of the group with any **neuropathic pain** was significantly lower than that of the group with nociceptive pain only (26.1 versus 20.4, p = 0.02). The score of the group with definite nociceptive pain alone (adjusted mean TOTPAR = 28.0) was significantly higher than scores of the groups with possible/probable nociceptive pain (TOTPAR = 19.9), mixed mechanisms (TOTPAR = 20.2), definite **neuropathic pain** alone (TOTPAR = 20.6), and possible/probable **neuropathic pain** alone (TOTPAR = 22.9).(ABSTRACT TRUNCATED AT 250 WORDS)

L39 ANSWER 40 OF 90 MEDLINE on STN
AN 68278368 MEDLINE
DN PubMed ID: 5654625

TI Pain in the face.
AU Miller H
SO British medical journal, (1968 Jun 8) 2 (605) 577-80.
Journal code: 0372673. ISSN: 0007-1447.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 196808
ED Entered STN: 19900101
Last Updated on STN: 20000303
Entered Medline: 19680801

L39 ANSWER 41 OF 90 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN DUPLICATE 5
AN 2004045505 EMBASE
TI Relieving effects of electroacupuncture on mechanical allodynia in **neuropathic pain** model of inferior caudal trunk injury in rat: Mediation by spinal opioid receptors.
AU Kim J.H.; Min B.-I.; Na H.S.; Park D.S.
CS B.-I. Min, Department of Physiology, College of Medicine, Kyung Hee University, #1 Hoegi-Dong, Dongdaemoon-Gu, Seoul, 130-701, Korea, Republic of. mbi@khu.ac.kr
SO Brain Research, (20 Feb 2004) 998/2 (230-236).
Refs: 54
ISSN: 0006-8993 CODEN: BRREAP
CY Netherlands
DT Journal; Article
FS 008 Neurology and Neurosurgery
030 Pharmacology
037 Drug Literature Index
LA English
SL English
AB The relieving effects of electroacupuncture (EA) on mechanical allodynia and its mechanism related to the spinal opioid system were investigated in a rat model of **neuropathic pain**. To produce **neuropathic pain** in the tail, the right superior caudal trunk was resected between the S1 and S2 spinal nerves. Two weeks after the surgery, EA stimulation (2 or 100 Hz, 0.3 ms, 0.2-0.3 mA) was delivered to Zusanli (ST36) for 30 min. The degree of mechanical allodynia was evaluated quantitatively by touching the tail with von Frey hair (2.0 g) at 10 min intervals. These rats were then subjected to an i.t. injection with one of the three specific opioid agonists in successive ways: the mu agonist (DAMGO 25, 50 and 100 pmol), the delta agonist (DADELT II 0.5, 1 and 2 nmol), and the kappa agonist (U50488H 5, 10 and 20 nmol) separated by 10 min in cumulative doses. During 30 min of EA stimulation, specific opioid antagonists were subjected to i.t. injection: the mu antagonist (β-FNA 5, 10 and 20 nmol), the delta antagonist (naltrindole 5, 10 and 20 nmol), and the kappa antagonist (nor-BNI 3, 6 and 12 nmol) separated by 10 min in cumulative doses. As a result, EA reduced the behavioral signs of mechanical allodynia. Two Hz EA induced a robust and longer lasting effect than 100 Hz. All three opioid agonists also showed relieving effects on mechanical allodynia. However, nor-BNI could not block the EA effects on mechanical allodynia, whereas β-FNA or naltrindole significantly blocked EA effects. These results suggest that the mu and delta, but not kappa, opioid receptors in the spinal cord of the rat, play important roles in mediating relieving effects on mechanical allodynia induced by 2 Hz EA. .COPYRGT. 2003 Elsevier B.V. All rights reserved.

L39 ANSWER 42 OF 90 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
AN 2004335684 EMBASE
TI Pharmacological management of metastatic boney pain.
AU Viney R.P.C.; Hayne D.; Ayra M.; Patel H.R.H.
CS Dr. H.R.H. Patel, Department of Urology, Guys Hospital, St Thomas Street, London SE1 9R, United Kingdom. hrhpatel@doctors.org.uk
SO Expert Opinion on Pharmacotherapy, (2004) 5/7 (1555-1563).
Refs: 39
ISSN: 1465-6566 CODEN: EOPHF7
CY United Kingdom
DT Journal; General Review
FS 008 Neurology and Neurosurgery
016 Cancer
033 Orthopedic Surgery
036 Health Policy, Economics and Management
037 Drug Literature Index
038 Adverse Reactions Titles
LA English
SL English
AB Many malignancies metastasise to the skeleton. This often results in a relatively unique pain process, which dramatically affects a patient's quality of life. With one in three members of the population likely to develop cancer at some stage in their lives, the prevalence of bone metastases is high. Despite the large financial investment on therapies for these patients, treatment is still suboptimal [1]. In this article, the various treatments available are reviewed. Opiates and bisphosphonates, the mainstays in current practise, are covered in detail, and evolving therapies that may shape future management are also discussed. 2004 .COPYRGT. Ashley Publication Ltd.

L39 ANSWER 43 OF 90 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
AN 2004433784 EMBASE
TI Headache in Guillain-Barre syndrome.
AU Pyati S.; Razis P.A.; Desai P.
CS P.A. Razis, Department of Anaesthesia, St. George's Healthcare NHS Trust, Blackshaw Road, London SW17 0QT, United Kingdom. platraz@tiscali.co.uk
SO Journal of Neurosurgical Anesthesiology, (2004) 16/4 (294-295).
Refs: 9
ISSN: 0898-4921 CODEN: JNANEV
CY United States
DT Journal; Article
FS 008 Neurology and Neurosurgery
024 Anesthesiology
037 Drug Literature Index
LA English
SL English
AB Severe headache in Guillain-Barre syndrome is rare. We report the management of a young patient with Guillain-Barre syndrome who suffered severe headache, which was not relieved by conventional analgesics. There was evidence of raised intracranial pressure. Insertion of lumbar drain and drainage of cerebrospinal fluid relieved her headache.

L39 ANSWER 44 OF 90 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
AN 2004082868 EMBASE
TI Headaches and vasculitis.

AU Younger D.S.
CS Dr. D.S. Younger, 715 Park Avenue, New York, NY 10021, United States. david.younger@med.nyu.edu
SO Neurologic Clinics, (2004) 22/1 (207-228).
Refs: 17
ISSN: 0733-8619 CODEN: NECLEG
CY United States
DT Journal; General Review
FS 008 Neurology and Neurosurgery
018 Cardiovascular Diseases and Cardiovascular Surgery
037 Drug Literature Index
038 Adverse Reactions Titles
LA English
SL English
AB Vasculitis is a spectrum of clinicopathologic disorders defined by inflammation of systemic and central nervous system (CNS) arteries and veins of differing caliber with variable tissue injury. At the onset of systemic vasculitis, headache can occur in association with constitutional symptoms without imminent danger to the individual. In the advanced stages of systemic vasculitis and in selected other vasculitic disorders, headache should arouse suspicion of CNS involvement and therefore warrant prompt evaluation and treatment to forestall progression and prevent cerebral ischemia and infarction.

L39 ANSWER 45 OF 90 EMBASE
on STN
AN 2004106951 EMBASE
TI Ongoing controversies in the pharmacological management of cancer pain.
AU Glare P.; Aggarwal G.; Clark K.
CS K. Clark, Palliative Care, Sydney Cancer Centre, Royal Prince Alfted Hospital, Missenden Road, Camperdown, NSW 2050, Australia. katherine.clark@email.cs.nsw.gov.au
SO Internal Medicine Journal, (2004) 34/1-2 (45-49).
Refs: 22
ISSN: 1444-0903 CODEN: IMJNAK
CY Australia
DT Journal; General Review
FS 006 Internal Medicine
016 Cancer
036 Health Policy, Economics and Management
037 Drug Literature Index
038 Adverse Reactions Titles
LA English
SL English
AB Pain management remains a problem in advanced cancer. Despite the ready availability of effective analgesia and good evidence to support the prescription of medications, concerns continue over the safety of this practice. The aim of the present paper was to review often-raised questions when considering the use of opioids, especially in cancer pain, to ascertain the levels of evidence that already exist to support opioid-prescribing practice and to identify areas where further research is needed.

L39 ANSWER 46 OF 90 EMBASE
on STN
AN 2004140787 EMBASE
TI Suppression of Acute Herpetic Pain-Related Responses by the κ-Opioid Receptor Agonist (-)-17-Cyclopropylmethyl-3,14β-dihydroxy-4,5α -epoxy-6β-[N-methyl-3-trans-3-(3-furyl) Acrylamido] Morphinan

Hydrochloride (TRK-820) in Mice.
AU Takasaki I.; Suzuki T.; Sasaki A.; Nakao K.; Hirakata M.; Okano K.; Tanaka T.; Nagase H.; Shiraki K.; Nojima H.; Kuraishi Y.
CS Dr. Y. Kuraishi, Department of Applied Pharmacology, Faculty of Pharmaceutical Sciences, Toyama Med. and Pharmaceutical Univ., 2630 Sugitani, Toyama 930-0194, Japan. kuraisiy@ms.toyama-mpu.ac.jp
SO Journal of Pharmacology and Experimental Therapeutics, (2004) 309/1 (36-41).
Refs: 34
ISSN: 0022-3565 CODEN: JPETAB
CY United States
DT Journal; Article
FS 030 Pharmacology
037 Drug Literature Index
LA English
SL English
AB (-)-17-Cyclopropylmethyl-3,14β-dihydroxy-4,5α-epoxy-6β-[N-methyl-3-trans-3-(3-furyl) acrylamido] morphinan hydrochloride (TRK-820) is a κ-opioid receptor agonist that has pharmacological characteristics different from typical κ-opioid receptor agonists. This study was conducted to determine the antiallodynic and antihyperalgesic effects of TRK-820 in a mouse model of acute herpetic pain and to compare them with those of the κ-opioid receptor agonist enadoline and the μ-opioid receptor agonist morphine. Percutaneous inoculation with herpes simplex virus type-1 induced tactile allodynia and mechanical hyperalgesia in the hind paw on the inoculated side. TRK-820 (0.01-0.1 mg/kg p.o.), enadoline (1-10 mg/kg p.o.) and morphine (5-20 mg/kg p.o.) dose dependently inhibited the allodynia and hyperalgesia, but the antiallodynic and antihyperalgesic dose of enadoline markedly decreased spontaneous locomotor activity. The antinociceptive action of TRK-820 (0.1 mg/kg) was completely antagonized by pretreatment with norbinaltorphimine, a κ-opioid receptor antagonist, but not by naltrexone, a μ-opioid receptor antagonist. Repeated treatment with morphine (20 mg/kg, four times) resulted in the reduction of antiallodynic and antihyperalgesic effects, whereas the inhibitory potency of TRK-820 (0.1 mg/kg) was almost the same even after the fourth administration. There was no cross-tolerance in antinociceptive activities between TRK-820 and morphine. Intrathecal and intracerebroventricular, but not intraplantar, injections of TRK-820 (10-100 ng/site) suppressed the allodynia and hyperalgesia. These results suggest that TRK-820 inhibits acute herpetic pain through κ-opioid receptors in the spinal and supraspinal levels. TRK-820 may have clinical efficacy in acute herpetic pain with enough safety margins.

L39 ANSWER 47 OF 90 EMBASE
on STN
AN 2003237043 EMBASE
TI Induction of pain facilitation by sustained opioid exposure: Relationship to opioid antinociceptive tolerance.
AU Ossipov M.H.; Lai J.; Vanderah T.W.; Porreca F.
CS F. Porreca, Depts. of Pharmacol./Anesthesiology, University of Arizona, Tucson, AZ 85724, United States. frankp@u.arizona.edu
SO Life Sciences, (27 Jun 2003) 73/6 (783-800).
Refs: 156
ISSN: 0024-3205 CODEN: LIFSAK
CY United States
DT Journal; Conference Article
FS 008 Neurology and Neurosurgery
030 Pharmacology

037 Drug Literature Index
038 Adverse Reactions Titles
052 Toxicology
LA English
SL English
AB Opioid analgesics are frequently used for the long-term management of chronic pain states, including cancer pain. The prolonged use of opioids is associated with a requirement for increasing doses to manage pain at a consistent level, reflecting the phenomenon of analgesic tolerance. It is now becoming clearer that patients receiving long-term opioid therapy can develop unexpected abnormal pain. Such paradoxical opioid-induced pain, as well as tolerance to the antinociceptive actions of opioids, has been reliably measured in animals during the period of continuous opioid delivery. Several recent studies have demonstrated that such pain may be secondary to neuroplastic changes that result, in part, from an activation of descending pain facilitation mechanisms arising from the rostral ventromedial medulla (RVM). One mechanism which may mediate such pain facilitation is through the increased activity of CCK in the RVM. Secondary consequences from descending facilitation may be produced. For example, opioid-induced upregulation of spinal dynorphin levels seem to depend on intact descending pathways from the RVM reflecting spinal neuroplasticity secondary to changes at supraspinal levels. Increased expression of spinal dynorphin reflects a trophic action of sustained opioid exposure which promotes an increased pain state. Spinal dynorphin may promote pain, in part, by enhancing the evoked release of excitatory transmitters from primary afferents. In this regard, opioids also produce trophic actions by increasing CGRP expression in the dorsal root ganglia. Increased pain elicited by opioids is a critical factor in the behavioral manifestation of opioid tolerance as manipulations which block abnormal pain also block antinociceptive tolerance. Manipulations that have blocked enhanced pain and antinociceptive tolerance include reversible and permanent ablation of descending facilitation from the RVM. Thus, opioids elicit systems-level adaptations resulting in pain due to descending facilitation, upregulation of spinal dynorphin and enhanced release of excitatory transmitters from primary afferents. Adaptive changes produced by sustained opioid exposure including trophic effects to enhance pain transmitters suggest the need for careful evaluation of the consequences of long-term opioid administration to patients.

L39 ANSWER 48 OF 90 EMBASE
on STN
AN 2003187998 EMBASE
TI [Opiates and their immunomodulation properties].
OPIATY A JEJICH IMUNOMODULACNI VLASTNOSTI.
AU Blahoutova V.; Zajicova A.; Wilczek H.; Holan V.
CS Dr. V. Holan, Ustav Molekularni Genetiky AV CR, Flemingovo namesti 2, 166 37 Praha 6, Czech Republic. holan@img.cas.cz
SO Casopis Lekaru Ceskych, (2003) 142/4 (244-247).
Refs: 38
ISSN: 0008-7335 CODEN: CLCEAL
CY Czech Republic
DT Journal; General Review
FS 008 Neurology and Neurosurgery
026 Immunology, Serology and Transplantation
030 Pharmacology
037 Drug Literature Index
040 Drug Dependence, Alcohol Abuse and Alcoholism
LA Czech

SL English; Czech
AB Opiates have been recently used for suppression of the **neuropathic pain** or to relieve pain in patients with cancer diseases. However, opiates are also used by drug abusers to achieve feeling of euphoria. These drugs influence not only the nervous system but they can also modulate many other physiological functions including those of the immune system. Since opioid receptors have been found on the surface of cells of the immune system, two possible mechanisms of opiate actions have to be considered. The first one represents a direct action of the opiates through the opioid receptors on immune cells; the second mechanism is mediated by the nervous system. The immunomodulatory properties of the opiates have been demonstrated in numerous models. Especially the enhanced sensitivity to viral and bacterial infections, observed in drug abusers, is accounted to the side effects of opiates. Experimental animal models have shown even more complex actions of opiates, which can lead to suppression as well as to stimulation of individual immunological parameters. Although proliferation of lymphocytes tested in vitro after application of opiates in vivo is generally reduced, production of the pro-inflammatory cytokines and some functions of macrophages can be enhanced. Effects of opiate action depend on the experimental model used, the drug dose, way of drug application, time of testing and on the tested immunological parameter. This article summarizes recent knowledge of effects of opiates on the functions of cells of the immune system. It also refers global problems of exploitation of illegal drugs and the importance of methadone in the substitution treatment.

L39 ANSWER 49 OF 90 EMBASE
on STN
AN 2003388175 EMBASE
TI [Long-term opioid treatment for chronic non-cancer pain].
DLOUHODOBA LECBA OPIOIDY U CHRONICKE NENADOROVE BOLESTI.
AU Lejcko J.; Machart S.; Skalkova H.; Bejvancicky S.
CS Dr. J. Lejcko, Univerzita Karlova, Lekarska Fakulta a FN, Anesteziologicko-Resuscitacni Klin., 304 60 Plzen, Czech Republic
SO Bolest, (2003) 6/3 (146-154).
Refs: 33
ISSN: 1212-0634 CODEN: BOLECA
CY Czech Republic
DT Journal; Article
FS 008 Neurology and Neurosurgery
017 Public Health, Social Medicine and Epidemiology
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LA Czech
SL Czech; English
AB Currently, therapy of cancer-related pain by strong opioids has been established as a widely accepted therapeutical approach. Experience with long-term opioid analgesia in patients with cancer pain has shown a highly favourable risk/benefit ratio. The biological background of chronic non-cancer pain is benign; however, the consequences of untreated chronic non-cancer pain are malignant. Undertreatment of chronic pain causes intense physical and psychological suffering and can destroy the patient's quality of life. Where standard therapeutic methods have failed, patients can be treated by administration of strong opioids. However, this approach is relatively new, unknown and use of opioids in the management of chronic non-cancer pain remains controversial. Life expectancy of chronic pain patients is temporarily unlimited which is why the horizon of opioid therapy is also unlimited. The influence of opioids on the body is very

complex. There is uncertainty as to what extent these agents can alter our psychological and physiological functions for truly long-term treatment. From the ethical point of view it is relatively questionable to conduct a long term double-blind, and placebo-controlled study in patients with chronic non-cancer pain. But how to gain valid information about this treatment modality? It seems that an acceptable solution might be to carry out observational, long-term, non-placebo, prospective and multicentre clinical trials. At the present time, a"database of opioids" as the background for data collection has been created in the Czech Republic. This system will posse its own www.domain and will be accessible for any interested pain centres.

L39 ANSWER 50 OF 90 EMBASE
on STN
AN 2003109632 EMBASE
TI Morphinan derivatives - A review of the recent patent literature.
AU Gagliardi S.; Dondio G.; Giardina G.A.M.
CS S. Gagliardi, NiKem Research Srl, Via Zambeletti 25, 20021 Baranzate di Bollate, Milan, Italy. stefania.gagliardi@nikemresearch.com
SO IDrugs, (1 Feb 2003) 6/2 (129-137).
Refs: 60
ISSN: 1369-7056 CODEN: IDRUFN
CY United Kingdom
DT Journal; General Review
FS 030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
036 Health Policy, Economics and Management
029 Clinical Biochemistry
008 Neurology and Neurosurgery
LA English
SL English
AB Alkaloids extracted from the Papaverum somniferum are among the most powerfully acting and clinically used drugs for diseases of the central nervous system, in particular for pain. The basic ring system, common to these opiate alkaloids, is the morphinan skeleton, which in the last 50 years has been chemically manipulated to obtain compounds with improved potency and increased selectivity toward different populations of opioid receptors. Despite a huge amount of research, interest surrounding these compounds is still high. This review will discuss the patent applications published from January 2001 to June 2002, focusing on new chemical entities that could become drugs over the next few years, new chemical processes for the production of the morphinans currently used in therapy, novel formulations and combined compositions.

L39 ANSWER 51 OF 90 EMBASE
on STN
AN 2001247202 EMBASE
TI Gabapentin: Resistant **neuropathic pain** and malignancy [3].
AU Ross J.R.; Waight C.; Riley J.
CS J.R. Ross, Roysl Marsden Hospital, Fulham Road, London, United Kingdom
SO Palliative Medicine, (2001) 15/4 (348-349).
Refs: 5
ISSN: 0269-2163 CODEN: PAMDE2
CY United Kingdom
DT Journal; Letter
FS 008 Neurology and Neurosurgery
016 Cancer

037 Drug Literature Index
038 Adverse Reactions Titles
LA English

L39 ANSWER 52 OF 90 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
AN 2001398242 EMBASE
TI Opioids in chronic pain.
AU Przewlocki R.; Przewlocka B.
CS R. Przewlocki, Dept. of Molecular Neuropharmacology, Institute of Pharmacology, 12 Smetna Street, 31-343 Krakow, Poland. nfprzewl@cyf-kr.edu.pl
SO European Journal of Pharmacology, (10 Oct 2001) 429/1-3 (79-91). Refs: 145
ISSN: 0014-2999 CODEN: EJPHAZ
PUI S 0014-2999(01)01308-5
CY Netherlands
DT Journal; General Review
FS 008 Neurology and Neurosurgery
030 Pharmacology
037 Drug Literature Index
LA English
SL English
AB The advance in our understanding of the biogenesis of various endogenous opioid peptides, their anatomical distribution, and the characteristics of the multiple receptors with which they interact open a new avenue for understanding the role of opioid peptide systems in chronic pain. The main groups of opioid peptides: enkephalins, dynorphins and β-endorphin derive from proenkephalin, prodynorphin and proopiomelanocortin, respectively. Recently, a novel group of peptides has been discovered in the brain and named endomorphins, endomorphin-1 and -2. They are unique in comparison with other opioid peptides by atypical structure and high selectivity towards the μ-opioid receptor. Another group, which joined the endogenous opioid peptide family in the last few years is the pronociceptin system comprising the peptides derived from this prohormone, acting at ORL1 receptors. Three members of the opioid receptor family were cloned in the early 1990s, beginning with the mouse δ-opioid receptor (DOR1) and followed by cloning of μ-opioid receptor (MOR1) and κ-opioid receptor (KOR1). These three receptors belong to the family of seven transmembrane G-protein coupled receptors, and share extensive structural homologies. These opioid receptor and peptide systems are significantly implicated in antinociceptive processes. They were found to be represented in the regions involved in nociception and pain. The effects of opioids in animal models of inflammatory pain have been studied in great detail. Inflammation in the periphery influences the central sites and changes the opioid action. Inflammation increased spinal potency of various opioid receptor agonists. In general, the antinociceptive potency of opioids is greater against various noxious stimuli in animals with peripheral inflammation than in control animals. Inflammation-induced enhancement of opioid antinociceptive potency is characteristic predominantly for μ opioid receptors, since morphine elicits a greater increase in spinal potency of μ- than of δ- and κ-opioid receptor agonists. Enhancement of the potency of μ-opioid receptor agonists during inflammation could arise from the changes occurring in opioid receptors, predominantly in affinity or number of the μ-opioid receptors. Inflammation has been shown to alter the expression of several genes in the spinal cord dorsal horn. Several studies have demonstrated profound alterations in the spinal PDYN system when there is peripheral inflammation or chronic arthritis. Endogenous dynorphin biosynthesis also

increases under various conditions associated with **neuropathic pain** following damage to the spinal cord and injury of peripheral nerves. Interestingly, morphine lacks potent analgesic efficacy in **neuropathic pain**. A vast body of clinical evidence suggests that **neuropathic pain** is not opioid-resistant but only that reduced sensitivity to systemic opioids is observed in this condition, and an increase in their dose is necessary in order to obtain adequate analgesia. Reduction of morphine antinociceptive potency was postulated to be due to the fact that nerve injury reduced the activity of spinal opioid receptors or opioid signal transduction. Our recent study with endogenous ligands of the μ-opioid receptor, endomorphins, further complicates the issue, since endomorphins appear to be effective in **neuropathic pain**. Identification of the involved differences may be of importance to the understanding of the molecular mechanism of opioid action in **neuropathic pain**, as well as to the development of better and more effective drugs for the treatment of **neuropathic pain** in humans.

L39 ANSWER 53 OF 90 EMBASE on STN
AN 2001000505 EMBASE
TI Drug treatment of **neuropathic pain**.
SO Drug and Therapeutics Bulletin, (2000) 38/12 (89-93).
Refs: 37
ISSN: 0012-6543 CODEN: DRTBAE
CY United Kingdom
DT Journal; Article
FS 008 Neurology and Neurosurgery
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LA English
SL English
AB **Neuropathic pain** results from damage to or dysfunction in the nervous system. The term usually refers to pain caused by a primary abnormality in the peripheral nervous system, while pain caused by damage to the central nervous system tends to be called central **pain**. Once established, **neuropathic pain** frequently runs a chronic course and can be severe and difficult to treat. Most doctors (but especially GPs, neurologists, neurosurgeons, oncologists and pain clinic specialists) will encounter patients with **neuropathic pain**. Management, ideally in a multidisciplinary pain-relief clinic, often involves the combined use of a range of pharmacological and non-drug approaches, the latter including transcutaneous electrical nerve stimulation, psychological treatments, and specialist procedures to stimulate, block or destroy discrete areas of the nervous system. Here, we review just the drug treatments for **neuropathic pain**.

L39 ANSWER 54 OF 90 EMBASE on STN
AN 95244320 EMBASE
DN 1995244320
TI **Painful** sciatic **neuropathy** after heroin overdose [1].
AU Gille M.; Delbecq J.; Depre A.; Van den Bergh P.
CS Department of Neurology, Clinique Ste Elisabeth, 206 Avenue de Fre,B-1180 Brussels, Belgium
SO Journal of Neurology, (1995) 242/7 (478-480).
ISSN: 0340-5354 CODEN: JNRYA

CY Germany
DT Journal; Letter
FS 008 Neurology and Neurosurgery
040 Drug Dependence, Alcohol Abuse and Alcoholism
LA English

L39 ANSWER 55 OF 90 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
AN 95036420 EMBASE
DN 1995036420
TI Central nervous system vasculitis secondary to infections, toxins, and neoplasms.
AU Giang D.W.
CS Department of Neurology, Univ. of Rochester Medical Center,Rochester, NY, United States
SO Seminars in Neurology, (1994) 14/4 (313-319).
ISSN: 0271-8235 CODEN: SEMNEP
CY United States
DT Journal; General Review
FS 004 Microbiology
006 Internal Medicine
008 Neurology and Neurosurgery
016 Cancer
040 Drug Dependence, Alcohol Abuse and Alcoholism
LA English

L39 ANSWER 56 OF 90 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
AN 93321625 EMBASE
DN 1993321625
TI Clinical teratology.
AU Ornoy A.; Arnon J.
CS Laboratory of Teratology, Dept of Anatomy and Embryology, Hadassah University Hospital, PO Box 1172,Kiryat Hadassah, Jerusalem, Israel
SO Western Journal of Medicine, (1993) 159/3 (382-390).
ISSN: 0093-0415 CODEN: WJMDA2
CY United States
DT Journal; General Review
FS 007 Pediatrics and Pediatric Surgery
021 Developmental Biology and Teratology
052 Toxicology
LA English
SL English
AB The field of teratology has become increasingly important in preventive medicine programs. By avoiding specific teratogenic agents, many birth defects can be prevented. In this review we will summarize the currently documented teratogenic agents in humans.

L39 ANSWER 57 OF 90 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
AN 93132520 EMBASE
DN 1993132520
TI Pain syndromes and their treatment.
AU Bowsher D.
CS Pain Research Institute, Walton Hospital,Liverpool L9 1AE, United Kingdom
SO Current Opinion in Neurology and Neurosurgery, (1993) 6/2 (257-263).
ISSN: 0951-7383 CODEN: CNENE8
CY United Kingdom
DT Journal; Article

FS 008 Neurology and Neurosurgery
030 Pharmacology
037 Drug Literature Index
LA English
SL English
AB Neurogenic pain (encompassing all types of **neuropathic** and central **pain**) is discussed. Experimental work is presented in a model in which the rat sciatic nerve is loosely ligatured. In **painful** human **neuropathies**, tricyclic antidepressants have been found to be effective in proportion to the degree they facilitate monoaminergic activity. Several papers also stress the importance of early treatment with amitriptyline or desipramine, and the ineffectiveness of analgesics, including narcotics. In nociceptive pain, recent findings in humans emphasize the importance of both the retroinsular (SII) and the anterior cingulate cortices in the conscious appreciation of pain. Opioid studies have revealed individual differences in the metabolism of morphine to its 3- and 6-glucuronosides; patients with nociceptive pain who respond poorly to morphine or diamorphine probably have a high 3:6 ratio. It has been pointed out that methadone may be useful in such cases, as it is not broken down to glucuronosides.

L39 ANSWER 58 OF 90 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
AN 92173728 EMBASE
DN 1992173728
TI Morphine responsiveness of chronic pain: Double-blind randomised crossover study with patient-controlled analgesia.
AU Jadad A.R.; Carroll D.; Glynn C.J.; Moore R.A.; McQuay H.J.
CS Oxford Regional Pain Relief Unit, Churchill Hospital,Oxford OX3 7LJ, United Kingdom
SO Lancet, (1992) 339/8806 (1367-1371).
ISSN: 0140-6736 CODEN: LANCAO
CY United Kingdom
DT Journal; Article
FS 037 Drug Literature Index
024 Anesthesiology
030 Pharmacology
LA English
SL English
AB There is controversy about whether the lack of response of some chronic pain to opioid treatment is absolute or relative. It is widely believed that nociceptive pain is responsive to opioids whereas **neuropathic pain** tends not to be. We have used a method of patient-controlled analgesia (PCA) with simultaneous nurse-observer measurement of analgesia, mood, and adverse effects to address these issues. Ten patients with chronic pain were given morphine at two concentrations (10 and 30 mg/ml) by PCA in two separate sessions in a double-blind randomised crossover study. Before the study a clinical judgment was made as to whether each **pain** was nociceptive or **neuropathic**. Seven patients showed good analgesic responses (more than 70 mm pain relief on a visual-analogue scale) of pain at rest, two patients poor responses (less than 30 mm pain relief), and one a moderate response with both concentrations (30-70 mm pain relief). The response to morphine was consistent (greater and faster relief with the higher concentration) in nine patients. Two patients had pain on movement that responded moderately to low-concentration morphine and well to the higher concentration. All patients with pains judged to be nociceptive showed good analgesic responses compared with half of those with **neuropathic pain**. There was no evidence that analgesic response in patients

with **neuropathic pain** were due to changes in mood.
This PCA method is a quick and efficient tool to determine the consistency of the analgesic response. Such consistency can guide the clinician as to whether continued or higher-dose opioid treatment will produce good analgesia. An inconsistent response points to the use of other pain-relieving strategies.

L39 ANSWER 59 OF 90 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
AN 91143130 EMBASE
DN 1991143130
TI Drug-induced myopathies.
AU Le Quintrec J.-S.; Quintrec J.-L.
CS Service d'Orthopedie, Hopital Cochin, 27 Rue du Faubourg Saint Jacques, 75014 Paris, France
SO Bailliere's Clinical Rheumatology, (1991) 5/1 (21-38).
ISSN: 0950-3579 CODEN: BCRHEZ
CY United Kingdom
DT Journal; General Review
FS 006 Internal Medicine
008 Neurology and Neurosurgery
031 Arthritis and Rheumatism
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LA English
SL English
AB Myopathies are not an unusual complication of drug therapy. The major symptoms in drug-induced myopathies are proximal muscle weakness, increased muscle enzyme levels, electromyographic changes and histological lesions. Some drug-induced myopathies are associated with neuropathy. Drug-induced myopathies can be classified according to the presence or absence of muscular **pain** and associated **neuropathy**.
Among **painless** myopathies, we can distinguish myopathies without neuropathy (corticosteroids), myopathies with neuropathy (colchicine, chloroquine and hydroxychloroquine) and myasthenic syndromes (D-penicillamine, anti-biotics, β-blockers). Among painful myopathies, the classification is similar: painful myopathies may or may not be associated with **neuropathies**. **Painful** myopathies include polymyositis (D-penicillamine, cimetidine, zidovudine) and other myopathies without polymyositis (clofibrate, statines, cyclosporin). Among the painful neuromyopathies, eosinophilia-myalgia syndrome is a recently described disorder associated with the use of L-tryptophan. Combinations of drugs (for example, a fibrate and a statine or cyclosporin and colchicine) can induce severe myopathies. If such drugs are used together a vigorous surveillance to detect any sign of myopathy is warranted. Instead of classifying drug-induced myopathies according to clinical features, a histological classification can be proposed. Many drugs can induce vacuolar myopathy (colchicine, chloroquine, amiodarone, cyclosporin, drugs causing hypokalaemia and lipid lowering agents), some others cause a mitochondrial myopathy (zidovudine) or a necrotizing myopathy as seen with vincristine.

L39 ANSWER 60 OF 90 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
AN 88085321 EMBASE
DN 1988085321
TI Prevalence and risk factors of HIV infections among drug users and drug-using prostitutes in Amsterdam.

AU Van Den Hoek J.A.R.; Coutinho R.A.; Van Haastrecht H.J.A.; Van Zadelhoff A.W.; Goudsmit J.
CS Municipal Health Service, Department of Infectious Diseases, University of Amsterdam, 1011 HW Amsterdam, Netherlands
SO AIDS, (1988) 2/1 (55-60).
ISSN: 0269-9370 CODEN: AIDSET
CY United Kingdom
DT Journal
FS 006 Internal Medicine
017 Public Health, Social Medicine and Epidemiology
026 Immunology, Serology and Transplantation
035 Occupational Health and Industrial Medicine
047 Virology
040 Drug Dependence, Alcohol Abuse and Alcoholism
LA English
SL English
AB In December 1985 we started a study to determine the prevalence and risk factors of HIV infection among drug users and drug-using prositutes in Amsterdam. Recruitment took place at methadone posts (not drug-free; i.e. a low-threshold programme on which some drug users continue to use hard drugs, but at a lower level) and the weekly evening sexually transmitted diseases (STD) clinic for drug-addicted prostitutes. Three hundred and ten drug users have so far been tested and interviewed. Eighty-one per cent reported intravenous drug use; 83% of the 166 females and 15% of the 144 men reported prostitution. Female prostitutes practised mainly vaginal and orogenital intercourse and reported frequent use of condoms (89% of vaginal and 64% of orogenital contact). Male prostitutes practised mainly orogenital and manual contact. At entry 88 of the 310 (28%) were HIV-antibody-seropositive; 85 of these 88 were intravenous drug users and three were male homosexuals. HIV-antigen was detected in two seropositive and one seronegative intravenous drug-user. Antibodies to HTLV-1 were found in four out of 308. Risk factors independently associated with HIV-antibody seropositivity among intravenous drug users were: frequency of borrowing used needle or syringe, date of first intravenous drug use, recent intravenous drug use, time living in Amsterdam and German nationality. Of medical history data, an attack of herpes **zoster** in the previous 5 years had the greatest value in the prediction of the presence of HIV antibodies (relative risk 20.90; 95% confidence interval 2.41-167.27). While the prevalence of HIV infection among drug users is increasing in Amsterdam, it seems to be occurring at a slower rate than in other European cities. It is encouraging that the majority (74%) of intravenous drug users in this study was aware of the danger of needle and syringe sharing and significant changes in lifestyle regarding the safer use of intravenous drugs were found. How this change will influence the further spread of HIV among this group remains to be seen.

L39 ANSWER 61 OF 90 EMBASE
on STN
AN 82136881 EMBASE
DN 1982136881
TI Oral methadone for relief of chronic pain from cancer.
AU Portnow J.M.; Corbett R.J.
CS Camden County Addict. Dis., Lakeland, NJ 08012, United States
SO New England Journal of Medicine, (1982) 306/16 (989-990).
CODEN: NEJMAG
CY United States
DT Journal
FS 037 Drug Literature Index
040 Drug Dependence, Alcohol Abuse and Alcoholism

LA English
AB The case has been made by Lasagna in the June 18 issue and by Walsh and Saunders in the December 3 issue for using short acting oral opiates rather than intravenous agents for the treatment of chronic pain and advanced cancer. With methadone the authors of this letter to the editor have also successfully detoxified patients with a variety of systemic illnesses (including Prinzmetal's angina, porphyria, and herpes **zoster**) who had become addicted inadvertently by their physicians' initial attempt at pain control. Thus, methadone maintenance has a much wider role in society than simply treating the heroin-addicted street population. With a long half-life, a large tissue reservoir, and a low rate of development of analgesic tolerance, it seems the drug for chronic incapacitating pain. The editors favor oral morphine because of its flexibility (the dosage can be rapidly adjusted if pain changes), the ease of administration in aqueous solution, and the ability to deliver a large dose in small volume. However, the authors' experience and the kinetic features of methadone suggest that it has a role as a single dose-a-day analgesic. Their claims should be examined by a controlled clinical trial comparing the pharmacokinetic features and clinical efficacy of oral methadone given either as a single dose or every eight hours in the pain of chronic cancer.

L39 ANSWER 62 OF 90 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
AN 2002:290530 BIOSIS
DN PREV200200290530
TI The effects of TRK-820, a kappa-opioid agonist, on **neuropathic pain**.
AU Hirakata, Mikito [Reprint author]; Takasaki, Ichiro; Suzuki, Tomohiko [Reprint author]; Nakao, Kaoru [Reprint author]; Okano, Kiyoshi [Reprint author]; Tanaka, Toshiaki [Reprint author]; Kuraishi, Yasushi; Nagase, Hiroshi [Reprint author]
CS Pharmaceutical Research Labs., Toray Ind., Inc., Kamakura, 248-8555, Japan
SO Japanese Journal of Pharmacology, (2002) Vol. 88, No. Supplement 1, pp. 89P. print.
Meeting Info.: 75th Annual Meeting of the Japanese Pharmacological Society. Kumamoto, Japan. March 13-15, 2002. Japanese Pharmacological Society.
CODEN: JJPAAZ. ISSN: 0021-5198.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
Conference; (Meeting Poster)
LA English
ED Entered STN: 15 May 2002
Last Updated on STN: 15 May 2002

L39 ANSWER 63 OF 90 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
AN 2001:87422 BIOSIS
DN PREV200100087422
TI Dermorphin-saporin targets tonic descending facilitation in the rostral ventromedial medulla to block and reverse **neuropathic pain**.
AU Burgess, S. E. [Reprint author]; Vanderah, T. W.; Mantyh, P. W.; Malan, T. P., Jr.; Ossipov, M. H.; Lappi, D.; Lai, J.; Porreca, F.
CS University of Arizona, Tucson, AZ, USA
SO Society for Neuroscience Abstracts, (2000) Vol. 26, No. 1-2, pp. Abstract No.-243.6. print.
Meeting Info.: 30th Annual Meeting of the Society of Neuroscience. New

Orleans, LA, USA. November 04-09, 2000. Society for Neuroscience.
ISSN: 0190-5295.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 14 Feb 2001
Last Updated on STN: 12 Feb 2002
AB The hypothesis that chronic pain from L5/L6 spinal nerve ligation (SNL) is due to tonic activation of descending pain facilitation mechanisms was explored by selective targeting mu (mu) opioid receptor expressing cells in the RVM (i.e., presumably, "ON" cells). Rats were treated with a single RVM injection of dermorphin (DERM)(mu agonist), saporin (SAP), or dermorphin-saporin conjugate (DERM-SAP) and responses to non-noxious (von Frey filaments) or noxious (Hargreave's test) stimuli characterized. DERM-SAP retained high affinity for mu receptors and acutely produced antinociception (tail-flick test), indicating agonist actions of the conjugate. Decreased staining of mu receptor-expressing cells was seen in superficial dorsal horn and in dorsal root ganglia 28 days after intrathecal injection of DERM-SAP, but not DERM or SAP. RVM DERM-SAP, DERM or SAP did not significantly alter baseline thresholds to von Frey filaments or noxious heat applied to the paw over 28 days. At day 28, RVM pretreated rats were subjected to sham- or SNL surgery and responses to tactile and heat stimuli monitored 7 days later (i.e., 35 days after the RVM pretreatment). DERM and SAP pretreated SNL rats showed the expected development of tactile allodynia and thermal hyperalgesia, while DERM-SAP pretreated rats did not. The RVM pretreatments did not alter responses in sham-operated controls. Administration of RVM DERM-SAP, but not SAP or DERM, to SNL rats showed full reversal of established allodynia/hyperalgesia by day 14. RVM pretreatment with beta-funaltrexamine (beta-FNA; opioid mu antagonist) prevented the antiallodynic and antihyperalgesic effects of subsequent DERM-SAP injection. These data, together with findings of blockade of SNL pain with RVM lidocaine or lesions of the dorsolateral funiculus, support the possibility of tonic activation of descending facilitation as a basis for chronic **neuropathic pain**.

L39 ANSWER 64 OF 90 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
AN 1999:270259 BIOSIS
DN PREV199900270259
TI Are opioids effective in relieving **neuropathic pain**?.
AU Dellemijn, Paul [Reprint author]
CS Department of Neurology and Clinical Neurophysiology, Saint Joseph Hospital, 5500 MB, Veldhoven, Netherlands
SO Pain, (April, 1999) Vol. 80, No. 3, pp. 453-462. print.
CODEN: PAINDB. ISSN: 0304-3959.
DT Article
General Review; (Literature Review)
LA English
ED Entered STN: 15 Jul 1999
Last Updated on STN: 15 Jul 1999
AB The purpose of this review is to identify important issues and to review the data that underlie the controversial effectiveness of opioids in relieving **neuropathic pain**. This controversy seems related to the use of multiple definitions of **neuropathic pain** together with its distinct mechanisms in both experimental animal models and human **neuropathic pain** syndromes, methodological shortcomings in available randomized controlled clinical trials, different methods of pain assessment, the inappropriate use of

terms like efficacy and responsiveness, differential responses in spontaneous versus evoked pains, interindividual differences to specific opioids and opioid doses, and duration of follow-up. New randomized controlled clinical trials with opioids in **neuropathic pain** are still needed. These studies should include larger patient samples with rigorously defined homogeneous **neuropathic pain** syndromes. Active placebo's mimicking side-effects should be included in the double-blind design, and control of unmasking should be performed. Individual titration of the opioid dose and active management of side-effects in long-term follow-up studies need to measure both pain relief and quality of life.

L39 ANSWER 65 OF 90 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
AN 1995:488414 BIOSIS
DN PREV199598502714
TI Involvement of delta-1-opioid receptors in the antinociceptive effects of mexiletine in mice.
AU Kamei, Junzo [Reprint author]; Saitoh, Akiyoshi; Kasuya, Yutaka
CS Dep. Pathophysiol. Therapeutics, Fac. Pharmaceutical Sci., Hoshi Univ., 4-41 Ebara 2-chome, Shinagawa-ku, Tokyo 142, Japan
SO Neuroscience Letters, (1995) Vol. 196, No. 3, pp. 169-172.
CODEN: NELED5. ISSN: 0304-3940.
DT Article
LA English
ED Entered STN: 9 Nov 1995
Last Updated on STN: 9 Nov 1995
AB The mechanisms of the antinociceptive effect of mexiletine were assessed by administering selective mu-, delta- and kappa-opioid receptor antagonists in diabetic and non-diabetic mice. Intraperitoneal administration of mexiletine, at doses of 10 and 30 mg/kg, produced dose-dependent antinociception in the tail-pinch test in both non-diabetic and diabetic mice. The antinociceptive effect of mexiletine in diabetic mice was significantly greater than that in non-diabetic mice. The antinociceptive effect of mexiletine did not result from the activation of mu- or kappa-opioid receptors in either non-diabetic or diabetic mice, since treatment with either beta-funaltrexamine, a selective mu-opioid receptor antagonist, or nor-binaltorphimine, a selective kappa-opioid receptor antagonist, was ineffective in blocking mexiletine-induced antinociception. The antinociceptive effect of mexiletine was significantly antagonized by naltrindole, a selective delta-opioid receptor antagonist, in both non-diabetic and diabetic mice. Furthermore, the antinociceptive effect of mexiletine was significantly reduced in both non-diabetic and diabetic mice following pretreatment with 7-benzylidenenaltrexone, a selective delta-1-opioid receptor antagonist, but not with naltriben, a selective delta-2-opioid receptor antagonist. These results suggest that delta-1-opioid receptor-mediated mechanisms may be involved in the antinociceptive effect of mexiletine.

L39 ANSWER 66 OF 90 USPATFULL on STN DUPLICATE 8
AN 2003:220301 USPATFULL
TI Method
IN Jackson, Karen, Sheffield, UNITED KINGDOM
PI US 2003153592 A1 20030814
US 6713470 B2 20040330
AI US 2003-349431 A1 20030122 (10)
RLI Continuation-in-part of Ser. No. US 2002-108659, filed on 27 Mar 2002, PENDING Continuation-in-part of Ser. No. US 2002-53962, filed on 22 Jan 2002, ABANDONED

DT Utility
FS APPLICATION
LREP ARTER & HADDEN, LLP, 1100 HUNTINGTON BUILDING, 925 EUCLID AVENUE, CLEVELAND, OH, 44115-1475
CLMN Number of Claims: 128
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 748
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB There is described a method of treatment of a patient requiring analgesia which comprises the separate, simultaneous or sequential administration of a therapeutically effective amount of an opioid analgesic, devazepide and a surfactant.

There is also described a monophasic pharmaceutical composition comprising an amount of devazepide effective in the enhancement of opioid analgesia and a pharmaceutically acceptable surfactant.

L39 ANSWER 67 OF 90 USPATFULL on STN DUPLICATE 9
AN 2002:92280 USPATFULL
TI Novel antioxidants
IN Avery, Mitchell Allen, Oxford, MS, UNITED STATES
Pershadsingh, Harrihar A., Bakersfield, CA, UNITED STATES
PI US 2002048798 A1 20020425
US 6664287 B2 20031216
AI US 2001-809518 A1 20010314 (9)
PRAI US 2000-189514P 20000315 (60)
DT Utility
FS APPLICATION
LREP Harrihar A. Pershadsingh, 404 Windsor Park Drive, Bakersfield, CA, 93311
CLMN Number of Claims: 19
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 4281
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB This invention comprises administering to a human or animal in need of treatment an effective amount of an antioxidant lipoic acid derivative and/or pharmaceutically acceptable salts and solvates thereof for the treatment or prevention of pathological (inflammatory, proliferative and degenerative diseases, e.g. diabetes mellitus, atherosclerosis, Alzheimer's disease and chronic viral diseases) and non-pathological (e.g. skin aging and wrinkle formation) conditions caused by oxidative damage. Methods of synthesizing novel antioxidant lipoic acid derivatives and their use in preventing or treating diseases or conditions caused by oxidative stress and other free radical mediated conditions are described. Another aspect of this invention is the use of these antioxidant compositions for the protection of skin from damage caused by ultraviolet radiation and dessication, and to provide improved skin feel by desquamating, cleansing and clarifying the skin. The compositions described in this invention increase cellular viability of epidermal cells, promote cytoprotection, and decrease the production of inflammatory mediators such as inflammatory cytokines in these cells. The antioxidant compositions are incorporated into sunscreen products, soap, moisturizing lotions, skin toners, and other skin care products.

L39 ANSWER 68 OF 90 USPATFULL on STN
AN 2004:280902 USPATFULL
TI Method and composition for potentiating an opiate analgesic
IN Wang, Zaijie, Oak Park, IL, UNITED STATES

PI US 2004220203 A1 20041104
AI US 2004-769536 A1 20040130 (10)
PRAI US 2003-446232P 20030210 (60)
DT Utility
FS APPLICATION
LREP MARSHALL, GERSTEIN & BORUN LLP, 6300 SEARS TOWER, 233 S. WACKER DRIVE, CHICAGO, IL, 60606
CLMN Number of Claims: 27
ECL Exemplary Claim: 1
DRWN 4 Drawing Page(s)
LN.CNT 1576
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Composition and methods of treating pain and reducing, reversing, or preventing tolerance to opiate analgesics are disclosed. The composition and method utilize an opiate analgesic and a calcium calmodulin kinase (CaMKII) inhibitor as active agents to treat pain in mammals, including humans.

L39 ANSWER 69 OF 90 USPATFULL on STN
AN 2004:274251 USPATFULL
TI Dispersible pharmaceutical composition for treatment of mastitis and otic disorders
IN Britten, Nancy Jean, Portage, MI, UNITED STATES
Waldron, Niki Ann, Kalamazoo, MI, UNITED STATES
Watts, Jeffrey L., Kalamazoo, MI, UNITED STATES
Hallberg, John Walter, Nashville, MI, UNITED STATES
Burns, John W., Antigo, WI, UNITED STATES
PI US 2004214753 A1 20041028
AI US 2004-795191 A1 20040305 (10)
PRAI US 2003-456201P 20030320 (60)
DT Utility
FS APPLICATION
LREP PHARMACIA & UPJOHN, 301 HENRIETTA ST, 0228-32-LAW, KALAMAZOO, MI, 49007
CLMN Number of Claims: 57
ECL Exemplary Claim: CLM-01-14
DRWN No Drawings
LN.CNT 2215
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A method is provided for treatment of an infective condition in a fluid-containing organ having a natural exterior orifice, such as the udder of a milk producing animal or an ear. The method comprises administering an antibacterial agent to the organ via the exterior orifice and administering in combination therapy with the antibacterial agent a second agent that is an anti-inflammatory agent, an analgesic and/or an antipyretic. The antibacterial agent and, optionally, the second agent, are administered as a pharmaceutical composition further comprising a vehicle that comprises an amphipathic oil that is water dispersible and ethanol insoluble, microcrystalline wax and a pharmaceutically acceptable non-aqueous carrier. Also provided is such a composition comprising the antibacterial agent and the second agent. The composition is readily dispersible in the fluid of the fluid-containing

L39 ANSWER 70 OF 90 USPATFULL on STN
AN 2004:240480 USPATFULL
TI Heteroaryl substituted tetrazole modulators of metabotrophic glutamate receptor-5
IN Cosford, Nicholas D P, San Diego, CA, UNITED STATES
Chen, Chixu, San Diego, CA, UNITED STATES
Reger, Thomas S, San Diego, CA, UNITED STATES

Roppe, Jeffrey R, Temecula, CA, UNITED STATES
Smith, Nicholas D, San Diego, CA, UNITED STATES
PI US 2004186295 A1 20040923
AI US 2004-491613 A1 20040402 (10)
WO 2002-US31294 20021001
PRAI US 2001-327132P 20011004 (60)
DT Utility
FS APPLICATION
LREP MERCK AND CO INC, P O BOX 2000, RAHWAY, NJ, 070650907
CLMN Number of Claims: 45
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 4657
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Tetrazole compounds substituted directly, or by a bridge, with a heteroaryl moiety containing N adjacent to the point of connection of the heteroaryl, are mGluR5 modulators useful in the treatment of psychiatric and mood disorders such as, for example, schizophrenia, anxiety, depression, and panic, as well as in the treatment of pain and other diseases.

L39 ANSWER 71 OF 90 USPATFULL on STN
AN 2004:216037 USPATFULL
TI Method of treatment
IN Jackson, Karen, Deepcar Sheffield, UNITED KINGDOM
PI US 2004167146 A1 20040826
AI US 2003-622492 A1 20030721 (10)
RLI Continuation-in-part of Ser. No. US 2003-349431, filed on 22 Jan 2003, GRANTED, Pat. No. US 6713470 Continuation-in-part of Ser. No. US 2002-108659, filed on 27 Mar 2002, PENDING Continuation-in-part of Ser. No. US 2002-53962, filed on 22 Jan 2002, ABANDONED
PRAI GB 2003-208129 20030409
DT Utility
FS APPLICATION
LREP PATENT ADMINSTRATOR, KATTEN MUCHIN ZAVIS ROSENMAN, 525 WEST MONROE STREET, SUITE 1600, CHICAGO, IL, 60661-3693
CLMN Number of Claims: 45
ECL Exemplary Claim: 1
DRWN 1 Drawing Page(s)
LN.CNT 459
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A method of treating a patient undergoing analgesic therapy which comprises the separate, simultaneous or sequential administration of a therapeutically effective amount of an analgesic and an analgesic sparing amount of devazepide.

There is also described the use of devazepide in the manufacture of a medicament which reduces the dose required for administration of an opioid analgesic and superpotentiates the effect of the analgesic.

L39 ANSWER 72 OF 90 USPATFULL on STN
AN 2004:185073 USPATFULL
TI Method of treatment
IN Jackson, Karen, Sheffield, UNITED KINGDOM
PI US 2004142959 A1 20040722
AI US 2004-752411 A1 20040107 (10)
RLI Continuation of Ser. No. US 2003-349431, filed on 22 Jan 2003, GRANTED, Pat. No. US 6713470 Continuation-in-part of Ser. No. US 2002-108659, filed on 27 Mar 2002, PENDING Continuation-in-part of Ser. No. US

2002-53962, filed on 22 Jan 2002, ABANDONED
PRAI GB 2002-1367 20020122
DT Utility
FS APPLICATION
LREP PATENT ADMINSTRATOR, KATTEN MUCHIN ZAVIS ROSENMAN, 525 WEST MONROE STREET, SUITE 1600, CHICAGO, IL, 60661-3693
CLMN Number of Claims: 128
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 749
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB There is described a method of treatment of a patient requiring analgesia which comprises the separate, simultaneous or sequential administration of a therapeutically effective amount of an opioid analgesic, devazepide and a surfactant.

There is also described a monophasic pharmaceutical composition comprising an amount of devazepide effective in the enhancement of opioid analgesia and a pharmaceutically acceptable surfactant.

L39 ANSWER 73 OF 90 USPATFULL on STN
AN 2004:185072 USPATFULL
TI Combination therapy for the treatment of pain
IN Herzberg, Uri, Bridgewater, NJ, UNITED STATES
Cortright, Daniel N., Orange, CT, UNITED STATES
Hurtt, Mark M., Wallingford, CT, UNITED STATES
Krause, James E., Madison, CT, UNITED STATES
PA Neurogen Corporation (U.S. corporation)
PI US 2004142958 A1 20040722
AI US 2003-718034 A1 20031119 (10)
PRAI US 2002-433363P 20021213 (60)
DT Utility
FS APPLICATION
LREP EDWARDS & ANGELL, LLP, P.O. BOX 55874, BOSTON, MA, 02205
CLMN Number of Claims: 59
ECL Exemplary Claim: 1
DRWN 4 Drawing Page(s)
LN.CNT 6137
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Compositions and methods are provided for the treatment of pain. Compositions and methods are further provided for inhibiting the development of tolerance to addictive therapeutic agents (especially narcotic analgesics) in patients treated with such agents; for minimizing adverse effects (e.g., dependence) resulting from treatment with such addictive agents; and for enhancing pain relief resulting from narcotic analgesic administration. The compositions generally comprise a nontoxic VR1 antagonist, optionally in combination with an addictive therapeutic agent. Patients may be treated with a VR1 antagonist before, during or after administration of the addictive therapeutic agent to prevent, decrease the severity of, delay or treat tolerance and/or other adverse effects of the addictive agent in the patient.

L39 ANSWER 74 OF 90 USPATFULL on STN
AN 2004:171456 USPATFULL
TI Methods for treating pain by administering a nerve growth factor antagonist and an opioid analgesic and compositions containing the same
IN Shelton, David L., Oakland, CA, UNITED STATES
Vergara, German J., Moraga, CA, UNITED STATES
PI US 2004131615 A1 20040708

AI US 2003-682332 A1 20031008 (10)
PRAI US 2002-417347P 20021008 (60)
DT Utility
FS APPLICATION
LREP MORRISON & FOERSTER LLP, 755 PAGE MILL RD, PALO ALTO, CA, 94304-1018
CLMN Number of Claims: 11
ECL Exemplary Claim: 1
DRWN 3 Drawing Page(s)
LN.CNT 2398
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention features methods for treating or preventing pain comprising administering an amount of a nerve growth factor antagonist and an amount of an opioid analgesic such that together they provide effective pain relief. The invention also features compositions comprising a nerve growth factor antagonist and an opioid analgesic and kits containing the same.

L39 ANSWER 75 OF 90 USPATFULL on STN
AN 2004:38089 USPATFULL
TI Transdermal delivery of analgesics
IN Klose, Kathryn Traci-Jane, Chelsea, AUSTRALIA
Colagrande, Felicia Maria, Brunswick, AUSTRALIA
Morgan, Timothy Matthias, Carlton North, AUSTRALIA
Finnin, Barrie Charles, Glen Iris, AUSTRALIA
Reed, Barry Leonard, Strathmore, AUSTRALIA
PA Monash University (non-U.S. corporation)
PI US 2004028625 A1 20040212
AI US 2003-428012 A1 20030502 (10)
RLI Continuation-in-part of Ser. No. US 2001-910780, filed on 24 Jul 2001, PENDING Division of Ser. No. US 1998-125436, filed on 18 Dec 1998, GRANTED, Pat. No. US 6299900 A 371 of International Ser. No. WO 1997-AU91, filed on 19 Feb 1997, UNKNOWN
PRAI AU 1996-8144 19960219
DT Utility
FS APPLICATION
LREP FOLEY AND LARDNER, SUITE 500, 3000 K STREET NW, WASHINGTON, DC, 20007
CLMN Number of Claims: 19
ECL Exemplary Claim: 1
DRWN 1 Drawing Page(s)
LN.CNT 574
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention provides a transdermal drug delivery system which comprises: a therapeutically effective amount of an analgesic; at least one dermal penetration enhancer, which is a safe skin-tolerant ester sunscreen ester; and at least one volatile liquid. The invention also provides a method for administering at least one systemic acting analgesic to an animal which comprises applying an effective amount of the analgesic in the form of the drug delivery system of the present invention.

L39 ANSWER 76 OF 90 USPATFULL on STN
AN 2004:31864 USPATFULL
TI Opioid pharmaceutical compositions
IN Simon, David Lew, Mansfield Center, CT, UNITED STATES
PI US 2004024006 A1 20040205
AI US 2003-628089 A1 20030725 (10)
RLI Continuation-in-part of Ser. No. US 2002-306657, filed on 27 Nov 2002, PENDING Continuation-in-part of Ser. No. US 2001-922873, filed on 6 Aug 2001, GRANTED, Pat. No. US 6569866 Continuation-in-part of Ser. No. US

1998-152834, filed on 14 Sep 1998, GRANTED, Pat. No. US 6271240 Continuation-in-part of Ser. No. US 1997-866334, filed on 30 May 1997, ABANDONED Continuation-in-part of Ser. No. US 1996-643775, filed on 6 May 1996, ABANDONED
DT Utility
FS APPLICATION
LREP David L. Simon, P.O. Box 618, 100 Cemetery Road, Mansfield Center, CT, 06250
CLMN Number of Claims: 13
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 3420
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention is directed in part to dosage forms comprising a combination of an analgesically effective amount of an opioid agonist analgesic and a neutral receptor binding agent or a partial mu-opioid agonist, the neutral receptor binding agent or partial mu-opioid agonist being included in a ratio to the opioid agonist analgesic to provide a combination product which is analgesically effective when the combination is administered as prescribed, but which is less analgesically effective or less rewarding when administered in excess of prescription. Preferably, the combination product affects an opioid dependent individual differently from an opioid naive individual, and has a diminished likelihood of being associated with a life-threatening adverse drug reaction, especially in the opioid dependent individual.

L39 ANSWER 77 OF 90 USPATFULL on STN
AN 2003:311899 USPATFULL
TI Compositions and methods of using them
IN Smith, Maree Therese, Queensland, AUSTRALIA
Brown, Lindsay Charles, Sinnamon Park, AUSTRALIA
Harvey, Mark Bradford Pullar, Queensland, AUSTRALIA
Williams, Craig McKenzie, Queensland, AUSTRALIA
PI US 2003219494 A1 20031127
AI US 2003-393050 A1 20030320 (10)
PRAI US 2002-366594P 20020320 (60)
DT Utility
FS APPLICATION
LREP MINTZ, LEVIN, COHN, FERRIS, GLOVSKY, AND POPEO, P.C., ONE FINANCIAL CENTER, BOSTON, MA, 02111
CLMN Number of Claims: 83
ECL Exemplary Claim: 1
DRWN 7 Drawing Page(s)
LN.CNT 1908
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention is directed to compositions and methods for inducing, promoting or otherwise facilitating pain relief. More particularly, the present invention relates to the use of a compound which either directly or indirectly prevents, attenuates or reverses the development of reduced opioid sensitivity, together with a compound which activates the opioid receptor that is the subject of the reduced opioid sensitivity, in methods and compositions for the prevention or alleviation of **pain**, especially in **neuropathic** conditions and even more especially in peripheral **neuropathic** conditions such as **painful** diabetic **neuropathy** (PDN).

L39 ANSWER 78 OF 90 USPATFULL on STN
AN 2003:201410 USPATFULL

TI METHOD OF TREATMENT
IN Gibson, Karen, Sheffield, UNITED KINGDOM
PI US 2003139396 A1 20030724
AI US 2002-108659 A1 20020327 (10)
RLI Continuation-in-part of Ser. No. US 2002-53962, filed on 22 Jan 2002, PENDING
DT Utility
FS APPLICATION
LREP ARTER & HADDEN, LLP, 1100 HUNTINGTON BUILDING, 925 EUCLID AVENUE, CLEVELAND, OH, 44115-1475
CLMN Number of Claims: 41
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 285
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB There is described a method of treatment of a patient suffering from constipation characterised in that the method comprises the administration of a therapeutically effective amount of devazepide.

There is also described a method of treatment of a patient requiring analgesia which comprises the separate, simultaneous or sequential administration of a therapeutically effective amount of an analgesic and a stool softening amount of devazepide.

The use of devazepide in the manufacture of a medicament is also described.

L39 ANSWER 79 OF 90 USPATFULL on STN
AN 2003:146760 USPATFULL
TI Method and composition for potentiating an opiate analgesic
IN Gulati, Anil, Naperville, IL, UNITED STATES
PI US 2003100507 A1 20030529
AI US 2002-301449 A1 20021121 (10)
PRAI US 2001-333599P 20011127 (60)
DT Utility
FS APPLICATION
LREP MARSHALL, GERSTEIN & BORUN, 6300 SEARS TOWER, 233 SOUTH WACKER, CHICAGO, IL, 60606-6357
CLMN Number of Claims: 30
ECL Exemplary Claim: 1
DRWN 7 Drawing Page(s)
LN.CNT 1146
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Composition and methods of treating pain and reducing or reversing tolerance to opiate analgesics are disclosed. The composition and method utilize an opiate analgesic and an endothelin antagonist as active agents to treat pain in mammals, including humans.

L39 ANSWER 80 OF 90 USPATFULL on STN
AN 2003:145924 USPATFULL
TI Packaging of immunostimulatory substances into virus-like particles: method of preparation and use
IN Bachmann, Martin, Winterthur, SWITZERLAND
Storni, Tazio, Viganello, SWITZERLAND
Maurer, Patrik, Winterthur, SWITZERLAND
Tissot, Alain, Zurich, SWITZERLAND
Schwarz, Katrin, Schlieren, SWITZERLAND
Meijerink, Edwin, Zurich, SWITZERLAND
Lipowsky, Gerd, Zurich, SWITZERLAND

Pumpens, Paul, Riga, LATVIA
Cielens, Indulis, Riga, LATVIA
Renhofa, Regina, Riga, LATVIA
PA Cytos Biotechnology AG (non-U.S. corporation)
PI US 2003099668 A1 20030529
AI US 2002-244065 A1 20020916 (10)
PRAI US 2001-318994P 20010914 (60)
US 2002-374145P 20020422 (60)
DT Utility
FS APPLICATION
LREP STERNE, KESSLER, GOLDSTEIN & FOX PLLC, 1100 NEW YORK AVENUE, N.W., SUITE 600, WASHINGTON, DC, 20005-3934
CLMN Number of Claims: 207
ECL Exemplary Claim: 1
DRWN 60 Drawing Page(s)
LN.CNT 7907
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention relates to the finding that virus like particles (VLPs) can be loaded with immunostimulatory substances, in particular with DNA oligonucleotides containing non-methylated C and G (CpGs). Such CpG-VLPs are dramatically more immunogenic than their CpG-free counterparts and induce enhanced B and T cell responses. The immune response against antigens optionally coupled, fused or attached otherwise to the VLPs is similarly enhanced as the immune response against the VLP itself. In addition, the T cell responses against both the VLPs and antigens are especially directed to the Th1 type. Antigens attached to CpG-loaded VLPs may therefore be ideal vaccines for prophylactic or therapeutic vaccination against allergies, tumors and other self-molecules and chronic viral diseases.

L39 ANSWER 81 OF 90 USPATFULL on STN
AN 2003:133508 USPATFULL
TI In vivo activation of antigen presenting cells for enhancement of immune responses induced by virus like particles
IN Bachmann, Martin F., Winterthur, SWITZERLAND
Lechner, Franziska, Zurich, SWITZERLAND
Storni, Tazio, Viganello, SWITZERLAND
PA Cytos Biotechnology AG (non-U.S. corporation)
PI US 2003091593 A1 20030515
AI US 2002-243739 A1 20020916 (10)
PRAI US 2001-318967P 20010914 (60)
DT Utility
FS APPLICATION
LREP STERNE, KESSLER, GOLDSTEIN & FOX PLLC, 1100 NEW YORK AVENUE, N.W., SUITE 600, WASHINGTON, DC, 20005-3934
CLMN Number of Claims: 194
ECL Exemplary Claim: 1
DRWN 20 Drawing Page(s)
LN.CNT 6522
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention relates to the finding that stimulation of antigen presenting cell (APC) activation using substances such as anti-CD40 antibodies or DNA oligomers rich in non-methylated C and G (CpGs) can dramatically enhance the specific T cell response obtained after vaccination with recombinant virus like particles (VLPs) coupled, fused or otherwise attached to antigens. While vaccination with recombinant VLPs fused to a cytotoxic T cell (CTL) epitope of lymphocytic choriomeningitis virus induced low levels cytolytic activity only and did not induce efficient anti-viral protection, VLPs injected together

with anti-CD40 antibodies or CpGs induced strong CTL activity and full anti-viral protection. Thus, stimulation of APC-activation through antigen presenting cell activators such as anti-CD40 antibodies or CpGs can exhibit a potent adjuvant effect for vaccination with VLPs coupled, fused or attached otherwise to antigens.

L39 ANSWER 82 OF 90 USPATFULL on STN
AN 2003:38188 USPATFULL
TI Combination of trimebutine with an opioid analgesic
IN Hamon, Jacques, Orsay, FRANCE
Roman, Francois, Vitry-sur-Seine, FRANCE
PI US 2003027835 A1 20030206
AI US 2001-980813 A1 20011101 (9)
WO 2000-EP13183 20001219
PRAI EP 1999-125752 19991223
DT Utility
FS APPLICATION
LREP Charles W Ashbrook, Warner Lambert Company, 2800 Plymouth Road, Ann Arbor, MI, 48105
CLMN Number of Claims: 29
ECL Exemplary Claim: 1
DRWN 13 Drawing Page(s)
LN.CNT 1461
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention provides a combination of of trimebutine [2-dimethylamino-2-phenylbutyl-3, 4, 5-trimethoxy-benzoate hydrogen maleate] or its corresponding stereoisomers with an opioid analgesic for the preparation of a medicament to prevent and/or treat pain or nociception.

L39 ANSWER 83 OF 90 USPATFULL on STN
AN 2003:4087 USPATFULL
TI Formulations of adenosine A1 agonists
IN Bountra, Charanjit, Stevenage, UNITED KINGDOM
Clayton, Nicholas Maughan, Stevenage, UNITED KINGDOM
Naylor, Alan, Stevenage, UNITED KINGDOM
PI US 2003004126 A1 20030102
AI US 2002-168189 A1 20020618 (10)
WO 2000-GB4885 20001219
PRAI GB 1999-30071 19991220
DT Utility
FS APPLICATION
LREP DAVID J LEVY, CORPORATE INTELLECTUAL PROPERTY, GLAXOSMITHKLINE, FIVE MOORE DR., PO BOX 13398, RESEARCH TRIANGLE PARK, NC, 27709-3398
CLMN Number of Claims: 9
ECL Exemplary Claim: 1
DRWN 2 Drawing Page(s)
LN.CNT 742
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention provides a method of treating conditions associated with pain and alleviating the symptoms associated therewith which comprises administering to a mammal, including man, an adenosine A1 agonist or a physiologically acceptable salt or solvate thereof and an opioid or a physiologically acceptable salt or solvate thereof. The present invention also provides pharmaceutical formulations and patient packs comprising said combinations.

L39 ANSWER 84 OF 90 USPATFULL on STN
AN 2003:81743 USPATFULL

TI Combination of a selective NMDA NR2B antagonist and an opioid analgesic
IN Boyce, Susan, Bishops Stortford, UNITED KINGDOM
PA Merck Sharpe & Dohme Limited, UNITED KINGDOM (non-U.S. corporation)
PI US 6538008 B1 20030325
WO 9944610 19990910
AI US 2000-622733 20000822 (9)
WO 1999-GB585 19990226
PRAI GB 1998-4885 19980306
DT Utility
FS GRANTED
EXNAM Primary Examiner: Fay, Zohreh; Assistant Examiner: Kwon, Brian-Yong S.
LREP Rubin, David, Rose, David L.
CLMN Number of Claims: 6
ECL Exemplary Claim: 1
DRWN 3 Drawing Figure(s); 3 Drawing Page(s)
LN.CNT 662
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A combination of a selective NMDA NR2B antagonist and an opioid analgesic is useful in the treatment of pain or nociception.

L39 ANSWER 85 OF 90 USPATFULL on STN
AN 2002:228329 USPATFULL
TI Benzamidine derivatives
IN Baxter, Ellen W., Glenside, PA, UNITED STATES
Nortey, Samuel O., Elkins Park, PA, UNITED STATES
Reitz, Allen B., Lansdale, PA, UNITED STATES
PI US 2002123489 A1 20020905
AI US 2001-14081 A1 20011211 (10)
PRAI US 2000-255658P 20001214 (60)
DT Utility
FS APPLICATION
LREP AUDLEY A. CIAMPORCERO JR., JOHNSON & JOHNSON, ONE JOHNSON & JOHNSON PLAZA, NEW BRUNSWICK, NJ, 08933-7003
CLMN Number of Claims: 34
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 1423
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Benzamidine derivatives are useful delta-opioid receptor modulators, agonists useful as analgesics and antagonists useful as immunosuppressants, antiinflammatory agents, agents for the treatment of neurological and psychiatric conditions, medicaments for drug and alcohol abuse, agents for treating gastritis and diarrhea, cardiovascular agents and agents for the treatment of respiratory diseases.

L39 ANSWER 86 OF 90 USPATFULL on STN
AN 2002:102482 USPATFULL
TI Prodrugs of NAALAdase inhibitors
IN Jackson, Paul F., Bel Air, MD, United States
Slusher, Barbara S., Kingsville, MD, United States
PA Guilford Pharmaceuticals Inc., Baltimore, MD, United States (U.S. corporation)
PI US 6384022 B1 20020507
AI US 1997-1667 19971231 (9)
RLI Continuation-in-part of Ser. No. US 1997-863624, filed on 27 May 1997, now patented, Pat. No. US 6046180 Continuation-in-part of Ser. No. US 1997-858985, filed on 27 May 1997, now patented, Pat. No. US 6025344 Continuation-in-part of Ser. No. US 1996-775586, filed on 31 Dec 1996,

now patented, Pat. No. US 5795877 Continuation-in-part of Ser. No. US 1996-778733, filed on 31 Dec 1996, now patented, Pat. No. US 5863536 Continuation-in-part of Ser. No. US 1996-665776, filed on 17 Jun 1996, now patented, Pat. No. US 5672592
DT Utility
FS GRANTED
EXNAM Primary Examiner: Lambkin, Deborah C.
LREP Lyon & Lyon LLP
CLMN Number of Claims: 85
ECL Exemplary Claim: 1
DRWN 19 Drawing Figure(s); 19 Drawing Page(s)
LN.CNT 4496
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to prodrugs of NAALADase inhibitors, pharmaceutical compositions comprising the same, and methods of using the same to treat glutamate abnormalities and prostate diseases.

L39 ANSWER 87 OF 90 USPATFULL on STN
AN 2001:233617 USPATFULL
TI PLURAL BIOLOGICAL SAMPLE ARRAYS, AND PREPARATION AND USES THEREOF
IN KREEK, MARY JEANNE, NEW YORK, NY, United States
LAFORGE, KARL STEVEN, NEW YORK, NY, United States
SPANGLER, RUDOLPH, NEW YORK, NY, United States
PI US 2001053849 A1 20011220
AI US 1999-334113 A1 19990616 (9)
DT Utility
FS APPLICATION
LREP DAVID A JACKSON ESQ, KLAUBER & JACKSON, 411 HACKENSACK AVENUE, HACKENSACK, NJ, 07601
CLMN Number of Claims: 4
ECL Exemplary Claim: 1
DRWN 8 Drawing Page(s)
LN.CNT 1671
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to the high throughput analysis of polymorphisms of a family of genes associated with addiction and alcohol dependence. Included are probes prepared by a variety of techniques, a sample plate that may utilize DNA chip-type technology. The invention is adapted to identify both physiological and genetic conditions of subjects so tested, and should provide a rapid and inexpensive means for accomplishing the same.

L39 ANSWER 88 OF 90 USPATFULL on STN
AN 2001:14480 USPATFULL
TI Tachykinin antagonist and an opioid analgesic effective at treating pain or nociception
IN Hill, Raymond George, Royston, United Kingdom
PA Merck Sharp & Dohme Limited, Hoddesdon, United Kingdom (non-U.S. corporation)
PI US 6180624 B1 20010130
AI US 1999-257414 19990225 (9)
RLI Division of Ser. No. US 849968, now patented, Pat. No. US 5880132
PRAI GB 1994-626102 19941223
DT Utility
FS Granted
EXNAM Primary Examiner: Jarvis, William R. A.
LREP Thies, J. Eric, Rose, David L.
CLMN Number of Claims: 4
ECL Exemplary Claim: 1

DRWN No Drawings
LN.CNT 3058
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB This invention relates to methods and compositions for treating pain and nociception in a patient by administering a combination of a morpholine or thiomorpholine tachykinin antagonist and an opioid analgesic.

L39 ANSWER 89 OF 90 USPATFULL on STN
AN 2000:149700 USPATFULL
TI Topical application of opioid analgesic drugs such as morphine
IN Elkhoury, George F., 1561 Ramillo Ave., Long Beach, CA, United States 90815
PI US 6143278 20001107
AI US 1998-28117 19980223 (9)
DT Utility
FS Granted
EXNAM Primary Examiner: Levy, Neil S.
LREP Millen, White, Zelane & Branigan, P.C.
CLMN Number of Claims: 6
ECL Exemplary Claim: 1
DRWN 2 Drawing Figure(s); 1 Drawing Page(s)
LN.CNT 837
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention is directed to methods and pharmaceutical compositions for the topical administration of opioid analgesic drugs such as morphine. In particular, the invention relates to topical administration of an opioid analgesic agent, e.g., morphine sulfate, in admixture with a skin- or mucosal-specific penetration enhancer, to produce a localized analgesic effect in inflamed or non-inflamed skin or mucosal tissue, and without a transdermal or transmucosal migration of opioid agent, e.g., into the systemic circulation.

L39 ANSWER 90 OF 90 USPATFULL on STN
AN 1999:30813 USPATFULL
TI Tachykinin antagonist and an opioid analgesic effective at treating pain or nociception
IN Hill, Raymond George, Royston, United Kingdom
PA Merck Sharp & Dohme Limited, Hoddesson, England (non-U.S. corporation)
PI US 5880132 19990309
WO 9620009 19960704
AI US 1997-849968 19970620 (8)
WO 1995-GB2931 19951215
19970620 PCT 371 date
19970620 PCT 102(e) date
PRAI GB 1994-26102 19941223
DT Utility
FS Granted
EXNAM Primary Examiner: Jarvis, William R. A.
LREP Thies, J. Eric, Rose, David L.
CLMN Number of Claims: 4
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 2583
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB This invention relates to methods and compositions for treating pain and nociception in a patient by administering a combination of a piperidine tachykinin antagonist and an opioid analgesic.